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EDITORIAL

The introduction of a new ophthalmic review at this particular time, when the world literature is more easily available to a greater number than ever before, requires an explanation. Prior to World War II the abstract sections of the Archives of Ophthalmology and the American Journal of Ophthalmology presented brief abstracts largely of clinical importance. The investigator, student or writer seeking a more comprehensive review, found the Zentralblatt für die Gesamte Ophthalmologie entirely adequate.

The development of Excerpta Medica and Ophthalmic Literature after the war made available a much greater variety of abstracts. These publications combined with the broader coverage of the abstract section of the American Journal of Ophthalmology gave the reader of English virtually every article of ophthalmic interest published in the world today. Any attempt to duplicate or parallel the function of these competently directed journals would be both futile and unnecessary.

Several years ago it occurred to Dr. F. Herbert Haessler, editor of the abstract section of the American Journal of Ophthalmology, that a review journal, directed toward the practitioner, composed of condensations rather than abstracts and combined with editorial evaluation, would be of unusual value. A study by Williams and Wilkins Company, the publisher of a number of outstanding medical journals, indicated a wide interest in such a publication and plans were made for the Survey of Ophthalmology. An untimely illness prevented Dr. Haessler from assuming the duties of editor but he contributed generously of his time and counsel in the development of the editorial policy and the organization of the staff.

The Survey of Ophthalmology is thus a review journal which differs from existing abstract sources in several respects. Digests of important ophthalmic articles derived from the world literature are presented together with editorial comment by recognized authorities. All articles selected for inclusion are presented in sufficient detail so that it is usually unnecessary for the reader to refer to the original. The editorial comment evaluates the importance of the contribution and indicates its application in either practice or theory. The articles are selected and the comment prepared with the requirements of the practitioner paramount.

Thus the history and the plan preceding the first issue of the Survey of Ophthalmology. It is the firm wish of everyone associated with this new journal to make a unique contribution so that all eye patients and those responsible for their care will be familiar with the latest methods and thought in ophthalmology and the related sciences. It would be most appreciated if each reader would write and suggest what changes are required in subsequent issues to make the Survey of Ophthalmology most valuable and most interesting to him.

FRANK W. NEWELL, *Editor*

Current Review

CURRENT ASPECTS OF OCULAR PHARMACOLOGY

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Pharmacology may be defined as that branch of biology that aims at a study of organic structures and function through the observation of changes produced by chemical agents. A pharmacologic agent is a chemical agent, which affects living protoplasm. Pharmacotherapeutics is a medical science which studies the influence of chemical agents or drugs on the therapy of various diseases. It is essential to differentiate between the action of drugs on living things and the practical use of drugs in disease. The former is a scientific study, the latter the application of the knowledge acquired by such a study to the sick patient. To succeed in the care of the sick the physician ophthalmologist must appreciate, learn and understand the facts and principles acquired by the pharmacologist. The ophthalmologist of the present is aware of the difficulties in evaluating new therapies. He has become cognizant of the necessity of adequate controls in both experimental and clinical studies. He automatically categorizes new therapeutic approaches into those which are based on poorly controlled studies or carelessly devised experiments, those which are still in the experimental stage, those that are of established value but do not improve on presently available measures, and those that are superior to any previously employed agents. There is an awareness of the necessity for understanding pharmacologic principles before instituting drug therapy in any patient.

The eye for many years has been the testing ground for innumerable agents. Much of our present knowledge of the neurohumeral theory of nerve impulse transmission was obtained here. It has become a favorate testing area for evaluating potential irritation of any new agent that might possibly come into contact with mucous membrane throughout the body.

The final goal of ocular pharmacology is a revelation of the nature of the primary interaction between drugs and cells of the eye to account for the specific quantitative alterations of cellular function.

SITES OF DRUG ACTION

When chemical agents are introduced into the body and reach the eye, they are not equally distributed among the various cells of the eye. The cells of the eye have different shapes and structures and different functions. The chemical agents are not distributed equally among the same kind of cell, for each of the

similar cells may have somewhat different functions. Each cell is not homogeneous but a most complicated structure. Drugs do not react with the cell as a whole but with a specific constituent of it. When a drug first makes contact with a cell, it obviously will encounter its surface. The surface of each cell is not homogenous but is made up of a mosaic contributed to by a variety of elements. There are believed to be specific surface elements often called receptors with which each effective drug first reacts. These receptors are part of a functional chain in that when they are influenced by the drug that contacts them, this union in turn leads to other changes causing alterations in other parts of the cell. Drug agents not only act at the surface of a cell, they may penetrate into the interior of the cell. Acetylcholine and epinephrine are thought to be agents which act exclusively by reaction with the surfaces of the cell. Since acetylcholine is acting on the surface of the cell, this would also tend to suggest that cholinesterase, which inactivates acetylcholine, should be at least partially located at the surface.

There are some compounds which by virtue of their size, seem unable to penetrate through the cell wall. Proteins are an example. Because of their molecular weight and volume, one would not expect them to diffuse through intact cell walls. However, they could get into cells by being phagocytosed by the cell or by injuring the cell membrane, thus altering its permeability. It is conceivable also that there may be agents which can penetrate a cell but still produce the bulk of their action through their activity at the cell surface. Methylene blue is able to enter cells but is thought to produce most of its atropine-like action through the portion which accumulates on the cell surface.

In studying the possible action of penicillin, Gale and Taylor found that gram positive bacteria are dependent to a large extent on the supply of specific amino-acids in the medium. He observed that the mechanism of the uptake of various amino-acids by some species of bacteria is different. Some, as lysine, pass through the medium by a passive diffusion process. Others, however, as glutamic acid are transported and accumulated actively, that is, by an energy-consuming metabolic reaction. This suggests that penicillin, which acts selectively against gram positive bacteria, might act here by inhibiting the uptake and accumulation of glutamic acid. Gale reasoned that this penicillin inhibition of the uptake of glutamic acid was secondary to the prevention of a synthetic process; i.e., a process tending to synthesize ribonucleic acid. Gramicidin also is thought to act in this manner. These drugs seem to interfere with energy-consuming synthetic mechanisms required for growth and multiplication of bacteria, but do not as a rule interfere with energy-yielding processes such as the oxidation and utilization of carbohydrates. These data suggest that, with many bacteria, the energy-consuming function required for synthetic processes such as growth and multiplication are much more sensitive to inhibitory drug influences than are the energy-yielding functions.

SELECTION OF DRUG SITE OF ACTION

Consideration must be given to the method by which drugs select the cells with which they are going to react. The affinity may depend ultimately on the

chemical structure of the drug or on its shape. The selection of the drug for a particular cell may depend on its physical and chemical properties, that is, its water, lipoid solubility, its surface activity, and due to these, its absorbability. Drugs may act on a purely physical basis. For example, methylcellulose in dilute solution protects the corneal surface from irritation. Also radioactive isotopes are used widely in many aspects of medical research, diagnosis and therapy. The emanations resulting from the disintegration of radioactive isotopes are measurable in extremely small amounts, thus making possible the use of isotopes as tracers in chemical reactions and in the studies of the distribution and excretion of isotope-containing compounds in the body. These emanations also have destructive properties which account for their effectiveness in the therapy of such conditions as hyperthyroidism and polycythemia rubra vera. The mechanism by which the emanations from the radioactive isotopes produce their effect is thought to be ionization of the target material. The differences in effectiveness of alpha, beta, gamma or neutron irradiation is due to differences in penetrability of the particles in the rays and the relative intensity of ionization produced along their path. The isotopes most commonly used are iodine-131, phosphorus-32, sodium-24 and carbon-14.

The biologic effect of an internally administered isotope is dependent on the nature and intensity of irradiation, the half-life of the isotope, its persistence in the body and the distribution pattern during the time it remains in the body.

Narcotic action is thought to be related to physico-chemical properties although the actual mechanism of narcosis is not known.

Alterations of one grouping in a molecule, by subtracting or adding a group or groups, may change the effect of the compound. Pentamethonium iodide is chiefly a ganglionic blocking agent, while decamethonium iodide has predominantly a curariform effect. One difference in these compounds is the number of CH_2 groups between the two ends and the molecule. However, our knowledge of the relationship between chemical configuration and pharmacologic action is still quite limited. The idea that a pharmacologic agent has a certain form that will allow it to fit together with the cell surface or substance with which it is going to act as a key fits into a lock was first postulated by Ehrlich.

Agents of quite different chemical structure may display the same affinity and possess the same action on specific cell substrate because their molecules have the same size and shape. Compounds may have different chemical properties yet, by virtue of their similar configuration, tie up the same enzymes or the same antibodies. No drugs can act by interfering with enzyme activity. They can do so by reacting directly with the enzyme or by competing with the enzyme for substances physiologically acted upon by the enzymes or for elements needed for the synthesis of the enzymes. The term, competitive inhibition, is one used if both the drug and its antagonist compete for the same site of attachment in the tissue. This may also be known as substrate competition, where the enzyme is competing with the drug for substances physiologically acted upon by the enzymes.

The majority of pharmacologic agents are active by virtue of an interference

with some enzymatic processes essential for the normal metabolism of the affected cell. Enzymatic reactions are readily influenced by enzyme, substrate and coenzyme concentrations, pH, temperature, and the presence of activators or inhibitors. Consequently, a drug affecting any of these factors may elicit a pharmacologic response. For example, arsenic and mercury combine with sulfhydryl groups, thus preventing the sulfhydryl-containing enzyme from further participation in the economy of the cells so poisoned. Lewisite gas does its damage to the ocular structures by the interference with the sulfhydryl-containing enzyme systems. British anti-lewisite (BAL) competes with the SH-containing enzymes for the arsenic of the lewisite gas. In this way it prevents the damage to the enzyme system.

An example of substrate competition is that of the interaction of acetylcholine and the enzyme cholinesterase. Eserine inhibits this action of cholinesterase on acetylcholine by competing with acetylcholine for the esterase. The activity of eserine is reversible in that a large amount of acetylcholine is able to displace the eserine from the esterase. Similarly, epinephrine may be destroyed by aminoxidase as acetylcholine is hydrolyzed by cholinesterase. Epinephrine may be protected from this destructive action of aminoxidase in a similar competitive way by ephedrine or cocaine. Similarly, another form of substrate competition or competitive inhibition is that brought about by compounds which are similar in structure to the essential elements found in enzymes. Thus, they compete with the enzymes for substances required in their own synthesis and for their own activity. Woods in 1940 demonstrated *in vitro* that inhibition of bacterial growth with sulfonamide could be overcome in a competitive manner by para-amino-benzoic acid. This led to the theory that para-amino-benzoic acid was an essential substance for a bacterial nutrition and that the sulfonamides, having a similar structure, competed with para-amino-benzoic acid for uptake by enzyme. It has been demonstrated that para-amino-benzoic acid is an essential growth factor in all sulfa-susceptible bacteria. It has also been shown that pteroyl-glutamic acid (folic acid) is another essential metabolite of many bacteria. Folic acid apparently requires para-amino-benzoic acid for its synthesis. Thus folic acid would protect bacteria from sulfonamides although it actually is not competing directly with it. The antagonism really lies between sulfonamides and para-amino-benzoic acid in regard to the formation of folic acid. There are many instances where an agent acts by inhibiting the synthesis of the essential metabolite and the inhibition can be overcome by the addition of that metabolite. The 2,4-diamino-pyrimidines of which Daraprim is an example compete for precursors of folic and folinic acid. Thus, there may be a depletion of folic acid in patients who have been taking Daraprim for a long period of time. This can be overcome by feeding the patient folic acid, demonstrating that the inhibition in the production of folic acid can be overcome by the addition of folic acid itself.

ORGAN-SPECIFIC DRUGS

Numerous studies have been attempted to account for the way in which some drugs act only on specific organs. For example, apomorphine, an alkaloid de-

rived from morphine, has in therapeutic doses no other effect than to sensitize the vomiting center. Therefore, it is reasonable to assume that this center must differ in some unknown way from all other centers. It is conceivable that these organ-specific agents are reacting with certain cell substances which may be called receptors. It is true that this action has to be a rapid one but enzymes have been known to react very quickly. It is known that the anti-esterases will affect certain organs but it is also well established that they do so by reacting with the cholinesterase lodged in and on these organs. Digitalis has a specific effect on heart muscle and it has recently been suggested that this may be an interference with enzyme activity. One can readily understand how the drugs which act on enzymes will cause a decrease in activity of the various structures so affected. It is somewhat difficult, perhaps, to understand how drugs which interfere with enzyme activity can lead to increased activity of the particular organ. Nevertheless, this does occur. It may be that by inhibiting certain enzyme systems, others are free to act.

Organ-specific drugs may produce their effect through methods other than primary reactions with an enzyme. The drug may actually alter the permeability of the cell membrane changing the polarity of the membrane, setting up an electrical potential. Some compounds act by competing with normal cell constituents. Atropine competes with acetylcholine, acetylcholine being a normally occurring substance. Quaternary ammonium bases, such as pentamethonium and decamethonium iodide compete with acetylcholine. Antihistaminic agents compete with histamine. Thus, organ-specific drugs might act by interfering with enzyme function by altering permeability of membranes or by competing with normal cellular constituents (Loewi, 1952).

SOURCES OF DRUGS

The discovery of the pharmacologic action or therapeutic usefulness of a substance can be made in many ways. The activity can be discovered by pure chance. Another approach is by the screening system in which one tries a large number of drugs in an effort to find a particular pharmacologic activity. Arsenicals and the sulfonamides were found in this way. Another is to search very carefully and meticulously for all therapeutic uses or actions of a given preparation. This is quite a time-consuming and extravagant method because there are so many different types and variations of pharmacologic actions. Very few substances in pharmacology have received complete evaluation. The literature is overwhelming in valuable compounds that have been known for many years before their important pharmacologic action was discovered. Sulfonamides, isonicotinic acid hydrazides and even some of the antibiotic substances would fall into this category.

DRUG METABOLISM

Many of the quantitative and qualitative differences in the action of two closely related drugs are due to differences in their metabolism in the body; particularly is this true in reference to ocular structures. The absorption and

distribution of a drug by the various tissues and fluids of the body and the persistence in the various tissues are extremely important in determining the activity of any agent. In ophthalmology the nature of the permeability of the blood-aqueous barrier is quite important, for such properties as diffusibility and solubility and degree of ionization of a drug may have a profound influence in determining the ability of an agent to penetrate or to fix on a particular cell. These factors have been stressed repeatedly in consideration of the antibiotic substances. It is well known that many antibiotics do not penetrate well into the eye when administered systemically, and that only by local application in high concentration can adequate tissue concentration be obtained in the intraocular structures. Differential solubility in lipids may be of importance. For example, an agent such as chloramphenicol, a lipoid soluble substance, penetrates into the intraocular tissues in a fashion superior to other antibiotics which have a greater water solubility. In experimental studies it is known that absorption and penetration of drugs may vary in different species of animals. For this reason, it is highly desirable to use as many species as possible in studying the distribution characteristics of any new compounds. Chemical tests may reveal the presence in the ocular tissues of a certain drug, but it is necessary for one to be certain that what he has found is still an active compound. Drugs may be broken down during their course through the body and reach the ocular tissues in an inactive form. There are variations in the rate at which a drug is broken down in the body. It is essential for one working in this field to have a knowledge of enzyme systems which may be involved in the metabolism of drugs. The distribution of the drug in the body will vary with the pathologic and physiologic states of the body and specific organ at the time of administration. For example, it is well known that the permeability of the blood-aqueous barrier will be increased in the presence of inflammation, so that some agents which do not penetrate well into the normal eye from the blood stream will have a better penetration in the presence of a local inflammatory reaction. The drug may be combined as an absorption complex onto some normal constituent of the body such as protein or serum or tissue. Such complexes may prolong the activity of the drug in delaying its excretion or detoxification. On the other hand, such a complex may lead to inactivation. The speed at which drugs are excreted from the body may be important for it may not allow high enough blood levels to be obtained for spill-over into the intraocular tissues. There are secondary agents which can be used to delay the excretion of certain compounds. Benemid will delay the renal excretion of penicillin, thus producing higher blood levels and perhaps increase the intraocular penetration of penicillin.

DRUG IDIOSYNCRASIES, SENSITIZATION AND TOLERANCE

Repeated administration of a drug is occasionally accompanied by either a decrease or increase in its action. The decrease in activity is referred to as an increase in drug tolerance. It may be due either to a change in the metabolism of the drug or change in the reactivity of the cell involved. An increase in activity may be due to accumulation of the drug due to slow excretion. Occasionally

the individual shows an unusual sensitivity or an idiosyncrasy to a drug. The idiosyncrasy may be such that the patient reacts to a dose of the drug which does not produce an effect in most individuals. The drug may produce hypersensitivity reaction. If the drug is not protein in nature in itself, it may produce an allergic reaction by combining with some protein in the tear or intraocular fluids and in that way, act as an allergen.

Theodore (1953) has stressed the necessity for an awareness that locally instilled eye medicaments do not produce only allergic reactions, but may cause simple irritation. This is especially so in regard to preparations of alkaloids used in the treatment of glaucoma and uveitis. The importance of this awareness is that the drug might be continued in use if it were prepared in a different fashion so that it would be less irritating; whereas, if it were an allergic reaction, an entirely new drug must be substituted. The irritation of a drug may be due not so much to itself but to one of its degradation products. This can often be avoided by the proper preparations of solutions which decrease the possibility of the appearance of degradation products. The signs of allergic reaction are easy to recognize. Those from an irritation reaction may range from hyperemia to necrosis, the most characteristic sign being the development of follicles. Usually the conjunctiva of the lower lid and adjacent bulbar conjunctiva show most evidence of the irritation. In this type of conjunctival reaction, epithelial scrapings do not reveal eosinophils but mostly mononuclear cells. Stronger irritants such as turpentine and lime may produce some eosinophils with many leukocytes.

DETERMINATION OF TOXICITY

Before attempting therapeutic use of a new drug it is absolutely essential to know something of its toxicity. Not only does the ophthalmologist have to know the toxicity of an agent for the rest of the body but he must know its local ocular peculiarities. One must know how it will act after short and long term administration and by various routes of administration. One cannot screen new agents too carefully, and must realize that toxicities may not always be apparent after initial studies. One can recall many examples, e.g., the development of cataracts in patients who were given 2-4-di-nitrophenol for purposes of weight reduction, the appearance of carcinoma in the liver of patients given thorotrast for diagnostic purposes as many as thirty years earlier, the development of jaundice after Thorazine, anaphylactic deaths with penicillin, and blood dyscrasias with Butazolidine. There is always a genetic effect in humans exposed to excessive amounts of irradiation. The closure of the tear ducts induced by Furmethide was not noted in the initial studies and did not become evident for many years after its introduction.

ADMINISTRATION METHODS WITH OCULAR PHARMACOLOGIC AGENTS

Drugs may be administered for ocular effect orally. Rectal administration is rarely used except for anesthetic purposes. All routes of parenteral administration are employed in ophthalmology; e.g., intradermal, subcutaneous, intramuscular, intravenous, and inhalation. Local administration is the most popular

method of utilizing ophthalmic drugs. Local applications to the eye may be in the form of drops, ointments, cotton packs, corneal baths, and subconjunctival injections. Galvanic currents can increase substantially the penetration of some ionizable drugs. The process is known as iontophoresis or electrophoresis. Agents can be injected directly into the anterior or vitreous chambers. They can also be injected retrobulbarly.

LOCAL OPHTHALMIC PREPARATIONS

The ideal ophthalmic solution should be one which is free and remains free of microorganisms for a reasonable length of time, should be non-irritating, of optimum physiologic activity, stable, of low toxicity, of low surface tension or of high wetting power, easily sterilized, compatible with other agents, and inexpensive. The hydrogen ion concentration of a solution and its maintenance are thought to be necessary to maintain best physiologic activity and stability of ophthalmic solutions and also to reduce irritability and facilitate corneal penetration. One may control and maintain the pH of a solution by buffering. A buffer solution is one whose pH cannot be seriously affected by the addition of reasonable amounts of weak acids or alkalis. The tears have a high buffering capacity and the corneal substance itself has some, so that the pH of ophthalmic solutions may not be as important in its immediate effect on the eye as it is in maintaining stability of the various ocular solutions. Many buffering solutions have been suggested. A very satisfactory one is that of Hind and Goyan (1954). This buffer is a mixture of anhydrous disodium phosphate so adjusted to be isotonic to physiologic saline. It is compatible with a preservative wetting agent such as benzalkonium chloride.

The penetration of most agents through the cornea can be facilitated by surface tension lowering agents or wetting agents. Swan believes that wetting agents enhance the chemical effectiveness of drugs administered to the eye by improving the contact of the drug with the corneal epithelium, by increasing the miscibility of the solution with the precorneal film and also by directly influencing the permeability characteristics of the epithelium.

It has been pointed out by Swan (1944) and by Leopold (1945) that detergents do have some toxic features. They may interfere with epithelial regeneration and if repeatedly applied, even in high dilution, may give rise to superficial corneal infiltrates that clear when the agent is withdrawn. There are many detergents which have been employed in ophthalmology, such as aerosol, Duponol M.E. dry, Phemerol, benzalkonium chloride, all of which have excellent wetting power and low toxicity and also have bacteriostatic and bacteriocidal properties. Of these, benzalkonium chloride has received the most widespread use in ophthalmology. It is, however, not effective against several strains of organisms, notably pseudomonas. It is a cationic agent and is inactivated by anionic detergents such as soap.

Theodore and Feinstein (1952), King (1953), Hasler (1939), Lawrence (1955), and McPherson and Wood (1949) have stressed the necessity of using something in ocular preparations to prevent them from becoming contaminated.

Sterilization of ophthalmic solutions can be done by mechanical filtration, by heat, by the use of chemicals or by passing a solution through a Berkefeld type filter. Boiling and autoclaving will kill pathogenic bacteria but may reduce the physiologic activity of the drug. Such measures insure sterility of the original preparation but do not maintain sterility unless the bottle is kept tightly sealed. A bottle which has to be opened several times a day, in which the dropper may become contaminated and then re-inserted into the bottle, will become contaminated. A number of substances have been recommended for use as bacteriocidal and bacteriostatic agents in ophthalmic solutions. They have been shown not to be too irritating to the human eye, nor incompatible with most ophthalmic drugs. Examples are boric acid, chlorbutanol, derivatives of benzoic acid such as 65 parts nitagin-M in combination with 35 parts of nitasol-M, benzalkonium chloride, Phemerol and mercurials such as mercuric nitrate. There are objections to most of these preservatives and antiseptics. Boric acid retards the growth of fungi but does not destroy pathogenic bacteria. Chlorbutanol may be irritating and is precipitated by pH above 7.5. Many of the wetting agents such as Zephiran (benzalkonium chloride) do not inhibit the growth of all strains of organisms, notably the pyocyaneus. Some of these wetting agents are incompatible with many of the alkaloids used in ophthalmology. For example, benzalkonium chloride is incompatible with physostigmine salicylate, and pilocarpine nitrate. Mercurial preservatives may induce hyersensitivity reactions (Vaughn, 1955; Murphy et al., 1955; Klein et al., 1954).

The studies of Riegelman, Vaughn and Okumoto suggest that the combination of Polymyxin B sulphate (1000 units per cubic centimeter) and benzalkonium chloride 1:10,000 appears to possess a broad spectrum and is rapidly bactericidal. They found chlorbutanol (0.5 per cent) to be second choice to this combination as a preservative (Riegelman et al., McPherson and Wood, 1949; Lawrence, 1955).

In order to reduce ocular irritation and possible damage to ocular tissues it has been suggested that all ophthalmic solutions be isotonic with tears. However, Hind and Goyan (1954), as well as others, have demonstrated that solutions of variable toxicity are rather well tolerated, particularly those which are the equivalent of 0.5 to 2 per cent sodium chloride solution. Most drugs as commonly employed are hypertonic, but owing to the protection of the tears and of the conjunctival fluid do not produce any significant irritation, or any corneal damage unless they are repeatedly instilled or used as large irrigations. Solutions which approximate 0.9 per cent and do not vary plus or minus 0.5 per cent in either direction are safe in this regard. The eyes can tolerate a wide change in osmotic pressure if the pH is controlled and a wide range in pH if the osmotic pressure is regulated (Martin and Mims, 1950).

In order to facilitate the passage of medicaments through the cornea into the eye one must consider the differential solubility of each compound. A water-soluble compound, if administered in an aqueous vehicle, tends to remain in the vehicle. A fat-soluble compound, however, if placed in an aqueous vehicle readily leaves this vehicle and enters the lipids of the cornea. It is desirable, therefore,

to place hydrophilic compounds in anhydrous vehicles. If the compound is highly lipid soluble, it should be administered in an aqueous solution.

The stability of the ophthalmic solutions has been thought to be related to its hydrogen ion capacity. Hind and Goyan have pointed out that the pH required for optimal ophthalmic activity may not correspond with the pH necessary for utmost stability. One may have to sacrifice slight physiologic activity in order to maintain solution stability. Morrison has noted that aqueous solutions of miotics remain stable for as long as six months, even when not buffered, and demonstrated that they can be sterilized by heating to 95°C. for one hour without significant loss of potency.

In an effort to obtain the ideal ophthalmic solution, that is, one free from irritation, possessing stability and sterility, one should not strive for these effects at the expense of pharmacologic effectiveness nor for pharmacologic effectiveness at the sacrifice of stability.

CHEMOTHERAPY IN CANCER

Large-scale investigation into the potentialities of chemotherapy are under way. The practical value of chemotherapy in tumors is confined to temporary palliation of the leukemias, lymphomas, and a few cancers of the prostate, breast, lung and ovary. Very little has been done with chemotherapy in ophthalmology. However, the potential for progress in this field is stimulating. Three different classes of agents have been used in the chemotherapy of cancer. The nitrogen-mustard type compound includes such agents as tri-ethylene melamine and tri-ethylene phosphoramide. These have been used with temporary success in metastatic cancer, leukemias and the lymphomas. The adrenal cortical hormones represent a second type of compound which has been found to be of value in chronic lymphatic leukemia and acute leukemia in young adults and children. The folic acid antagonists constitute the third group, and have had remarkable temporary effects in acute leukemia in children. Examples of such compounds are Aminopterin and amethopterin as well as 6-mercaptopurine. All of these agents may have considerable immediate success, but all eventually fail to hold the disease in check. The final failure appears to be due to development of resistance by the neoplastic cell with the loss of certain specific quantitative differences between it and the normal cell. Eventual studies may indicate the mechanism for this development of resistance. Vogel has developed a method for implanting tumors in the fundus of the eye which may prove helpful in evaluating these chemotherapeutic agents in ocular tumors. Reese et al. suggest that the combination of radiation and triethylene melamine are synergistic in the therapy of retinoblastoma. TEM can be given orally. The blood and platelet count must be watched closely. Such an agent may lengthen the survival time of these patients (Reese et al., 1955).

ENZYMES

Several enzymes are under study for their therapeutic value in ophthalmology, namely, hyaluronidase, streptokinase and streptodornase.

Hyaluronic acid, a muco-polysaccharide, is found in the ground substance of connective tissue, the vitreous humor, synovial fluid and umbilical cord, as well as being a constituent of the mucoid of the cornea. Hyaluronidase is an enzyme which depolymerizes hyaluronic acid. This enzyme therefore breaks down the tissue barrier of the connective tissue to a certain degree. This activity has been used to increase the spread of varied injected anesthetics. Hyaluronidase is found as one of the extracellular products of streptococci, and other bacterias such as pneumococcus. It has been demonstrated that the body can produce specific antibodies against the hyaluronidase of streptococcal origin (Leopold and Dickinson, 1954).

The weight of evidence suggests that the intraocular use of hyaluronidase may be dangerous and without great merit for the clearing of intraocular hemorrhage (Harris, 1955).

Ingenious studies by Barany and others have determined the influence of hyaluronidase on the resistance to outflow of intraocular fluid provided by the chamber angle. The weight of the *in vivo* studies available suggest that neither the hyaluronidase inhibitor (trigentisic acid) nor the injection of hyaluronidase into the anterior chamber or vitreous or subconjunctually, influenced significantly the intraocular pressure clinically. (Von Sallman, 1955).

Streptokinase, derived from streptococcus, is the name for streptococcal fibrinolysin. Streptodornase is a streptococcal desoxyribonuclease. Both of these substances have the property of dissolving solid sediment made up of fibrin and desoxyribonucleoprotein. Streptokinase probably produces its activity by stimulating the formation of a fibrinolytic enzyme, from a normal plasma constituent, called plasminogen. These agents might aid in the absorption of intraocular hemorrhage if injected into the anterior chamber of the eye. However, these compounds are presently available, are toxic and must be used in dilute concentrations for such purposes. The toxicity of the streptodornase-streptokinase preparations may be due to impurities such as hyaluronidase. These agents disappear rapidly from the anterior chamber following injection. Their lytic activity is of short duration (O'Rourke, 1955). The compounds do have the ability of breaking up necrotic tissue and therefore may be of value when locally instilled in the conjunctival cul-de-sac for aiding in the debridement of chronic corneal ulcers (Portfolio, 1954).

Trypsin is a proteolytic enzyme which may have a greater range of activity against proteins than the combination of streptokinase-streptodornase. It lyses fibrin readily and has been shown to break intravascular clots. It also may be useful for clearing up necrotic debris and exudates of corneal ulcers, and is reported as being of value in the breaking up of thrombi in the central retinal vein. There is not sufficient data available at the present time to determine its value in the therapy of central vein thrombosis or to estimate properly its toxicity when locally injected into the chambers of the eye or instilled into the cul-de-sac (Leopold, 1952). The evidence that intramuscular trypsin may be of value in ophthalmology is not convincing (Harris, 1955).

ANTI-ENZYMES

A number of anti-enzymes have been employed in ophthalmology. One could include a drug such as eserine or di-isopropyl fluorophosphate which inhibits the enzyme cholinesterase. A substance which inhibits hyaluronidase, trigentisic acid was found not to have any effect on the intraocular pressure. Another anti-enzyme which has received a great deal of attention in ophthalmology recently has been the carbonic anhydrase inhibitors such as acetoazoleamide, also known as Diamox.

The enzyme carbonic anhydrase is widely distributed in the human body. It has been described as being present in the lens by Bakker in 1948; in the iris and ciliary body by Leiner in 1943, and subsequently by Wistrandt in 1951 and by Green et al. in 1954.

Acetazoleamide affects many secreting organs. For example, it may alter the salivary gland activity, decreasing the sodium bicarbonate concentrations of the saliva (Niedermeier, et al., 1955). The composition of sweat is not altered by carbonic anhydrase inhibitors (Kleeman, et al., 1955). The kidney tubular function is markedly affected by acetazoleamide. This brings about the excretion of an alkaline urine containing increased quantities of sodium and potassium (Leaf, et al.). For this reason the drug has been proved useful as a diuretic in congestive heart failure and in other conditions where extracellular salt accumulation has developed. Following its extensive use decrease in the bicarbonate content of the plasma occurs.

It is well known to ophthalmologists that when Diamox is administered systemically, either intravenously or orally, it has a profound ocular hypotensive action, particularly when the initial pressure has been abnormally elevated. (Becker, 1954; Grant and Trotter, 1954; Breinan and Gortz, 1954; Leopold and Dickinson, 1954; Leopold and Carmichael, 1955).

Mode of Action. The drug appears to produce its intraocular effect by reducing the inflow of intraocular fluid and except for the report of Kleinert does not appear to have any action at the present time on the facility of outflow (Becker, 1954; Grant and Trotter, 1954). There is pro and con evidence that this agent inhibits carbonic anhydrase activity in the ciliary body (Green et al., 1954) and it may be exerting its influence on the formation of intraocular fluids through its inhibitory properties on this enzyme. Becker has pointed out that the degree of the resulting fall in intraocular pressure depends on the extent of inhibition of intraocular fluid formation produced by the agent and the facility of outflow mechanism. All of the investigators to date have agreed that Diamox produces only a temporary effect and the drug must be continued in order to prolong its pressure-lowering action.

Method of Administration. The drug can be administered orally as uncoated or enteric-coated tablets. The usual length of action of a 250 mgm. uncoated tablet is approximately up to six hours. The enteric coated tablets have been devised to give a more prolonged action, lasting as long as 12 hours. A combined tablet of an uncoated portion and a coated portion would give rise to immediate action

and also a more prolonged one. Such a preparation is now being made available. At the present time the uncoated tablet can be used as 250 mgm. four times daily or as much as 500 mgm. four times daily or as little as 125 mgm. daily, depending on the particular situation that exists. By using the combined tablet one might be able to administer the drug only twice each day in severe cases and obtain an equally effective degree of action.

The intravenous route of administration is usually employed in those patients in whom one is desirous of obtaining an extremely rapid effect on the ocular pressure, particularly in those individuals who are vomiting or unable to retain ingested material. The dosage for such individuals is 250 mgm. given in 3 cc. of sterile distilled water, repeated in two hours. This should be followed by oral administration as soon as the patient is able to take the drug in that fashion.

Dosage for Long-Term Therapy. One can determine the dosage of Diamox required by tonometry, by measuring the diurnal fluctuations throughout a 24- to 48-hour period and by the use of tonography. It is generally believed that short-term Diamox administration is a most effective adjunct to other means of therapy in the treatment of acute primary and secondary glaucoma as well as in the help of long-term therapy of chronic glaucoma.

Side Effects. The majority of patients will show evidence of paresthesias, gastrointestinal symptoms such as anorexia and weight loss, fatigue, drowsiness, and renal colic. Sometimes patients become confused from the drug. In no instance has ocular dysfunction been reported from use of the drug. There is always the possibility of allergic reactions as this drug is a derivative of the sulfonamides.

Diamox should be considered as an agent which does not attack the basic fault in glaucoma but controls the pressure by reducing the inflow of fluid. Measures which will increase the outflow of aqueous humor must still be employed. Diamox may be used in chronic glaucoma cases where other measures have failed or where because of age, serious illness, sensitivity to other agents, such methods that would reduce the resistance to outflow of intraocular fluid could not be employed. Anyone who employs this chronic form of therapy with Diamox should be well aware of the side effects and should keep the patient under close surveillance. (Leopold and Carmichael, 1955; Becker and Middleton, 1955; Breinin and Görtz, 1954; Grant and Trotter, 1954; Green et al., 1954; Becker, 1954; Kleinert, et al.)

CHEMOTHERAPY AND ANTIBIOTICS

One of the most miraculous achievements of modern medical research has been the development of chemotherapy and of antibiotics. The rapidity with which new agents have appeared and have been made available has been overwhelming. Although many of these agents have saved innumerable eyes that would have been lost by infection, it is increasingly evident that many eyes still succumb to infection. Both Leopold (1952) and Callahan (1953) have called attention to the limitations of therapy for intraocular infections, particularly those occurring after extraction of intraocular foreign bodies and intraocular surgery.

Antibiotic Problems. The use of antibiotics has brought forth new clinical

problems. All can produce hypersensitivity. Deaths have resulted from penicillin in this manner. Streptomycin produces aural damage; Aureomycin, Terramycin (chlor-tetracycline and oxytetracycline) and chloramphenicol produce gastrointestinal disorders. These latter agents rarely produce hypersensitivity reactions but are frequently associated with overgrowth of *Candida albicans* and sometimes with the overgrowth of *Micrococcus pyogenes*. The latter may be responsible for diarrhea. Chloramphenicol produces hematopoietic depression, in a small percentage of patients, and agents such as bacitracin, neomycin and polymixin may be nephrotoxic when systemically administered. Neomycin, additionally, has ototoxicity.

A major antibiotic problem is that of organism resistance and superinfection. Not infrequently antibiotics have been used in the treatment of specific infection over a long period of time, only to have some resistant strain of organism or nonsusceptible strain proliferate during therapy, and produce a new infection.

Selection of Antibiotic for Intraocular Infection. In the selection of antibiotics for therapy it is helpful to know the etiologic organism and its *in vitro* sensitivity to various antibiotics. In dealing with various intraocular infections, this is possible only rarely. Cultures of intraocular fluids are frequently negative, and if one waits 24 hours for the return of culture studies before starting therapy, the infection becomes more deeply intrenched and more difficult to overcome. Therefore, in dealing with an intraocular infection, one must use a broad spectrum antibiotic or antibiotics in a dosage which he is sure will produce an effective intraocular concentration of the antibiotic. This may require large dosages injected subconjunctivally or intraocularly, or massive doses administered systemically. If no improvement occurs in 24 hours, a switch to another antibiotic or antibiotic combination should be made. One must be aware of the possibility of encountering resistant organisms to each antibiotic. Therefore, every ophthalmologist should know alternative antibiotics and antibiotic combinations, and dosage schedules which will allow adequate intraocular penetration for each. The selection of combinations of antibiotics can be additive, synergistic, indifferent or antagonistic. By using combinations of the proper antibiotics, one may broaden the antibacterial spectrum, diminish the frequency of the development of resistant strains, and by using smaller doses of each of the antibiotics reduce the individual toxicity. One should not employ combinations that are unknown in their activity, as the combination may be impotent clinically. Use a single agent whenever it has a chance against the infection. One should always employ an adequate dosage schedule.

On the basis of penetration studies in experimental (Hallett et al., 1955; Abraham and Burnett, 1955) and human eyes (Abraham and Burnett, 1955; Leopold, 1951) Abraham and Burnett have suggested that tetracycline and chloramphenicol are satisfactory agents for ocular infections. Both agents penetrate well from the blood stream into the human eye following oral administration. Both possess broad antibacterial activity and rarely show cross resistance. An organism resistant to tetracycline would not necessarily be resistant to chloramphenicol.

Because of the possibility of bone marrow depression with chloramphenicol

and in spite of its better intraocular penetration following systemic administration, Abraham and Burnett feel that tetracycline should be the drug of choice for prophylactic and initial therapy of ocular infections. Chloramphenicol should be reserved for the intraocular infection that fails to respond to tetracycline and where some other antibiotic or chemotherapeutic agent has not been shown to possess greater activity against the infecting organism. A priming dose of 3 gm. and 500 mgm. every 6 to 8 hours should be adequate for oral administration of either tetracycline or chloramphenicol. A smaller priming dose for chloramphenicol might be adequate.

Anti-Toxoplasmosis Agents. If a method can be found for establishing the diagnosis in the acute stage of the infection, there is a reasonable hope that many of the new chemotherapeutic agents effective against the experimental toxoplasmosis infections will be helpful in human cases. Several drugs have been tested in the laboratory for their efficacy, namely the sulfonamides, the 2,4-diamino-pyrimidines, the sulfones and the antibiotics, and combinations of these. Of the antibiotics, Aureomycin appears to have some anti-toxoplasmic activity, and to a lesser extent, Terramycin, chloramphenicol and fumagilin. Penicillin, streptomycin, neomycin, and viomycin have failed to show any activity against the toxoplasma protozoa. There is considerable experimental evidence that the sulfonamides, particularly sulfadiazine, are definitely active against the toxoplasma in experimental animals. The 2,4-diamino-pyrimidines appear to have greater effectiveness against toxoplasma, as well as great anti-malarial activity. Results with these drugs appear to differ from the experimental results with sulfonamides in that there is an absence of the late returns of parasitic activity found after the use of sulfonamides. Daraprim is one of the 2,4-diamino-pyrimidine compounds (Eyles and Coleman, 1955).

It must be realized that the experimental work with these agents has dealt with acute infection. In all probability the agents are able to work best on actively growing toxoplasmal protozoa. There is considerable question whether they will be effective against chronic infection in which the organisms are multiplying slowly, if at all. Nevertheless, it is encouraging to realize that there are compounds available that may be helpful against toxoplasmosis.

Dangers of Prophylactic Therapy. There is no question concerning the value of prophylaxis against ophthalmia neonatorum. There still is some question as to whether or not antibiotics will replace the Credé prophylaxis. This problem has not been settled completely.

The question of the prophylactic use of antibiotics in ocular surgery has not been answered. There is always the danger when drugs are used prophylactically that a resistant strain may develop and be responsible for infection. One cannot predict whether or not prophylactically employed antibiotics will facilitate the rapid growth of resistant strains. Nevertheless, the use of prophylactic agents will reduce any possible infection by contaminants which are susceptible to the agent employed.

Most of the secondary infections which occur after ocular surgery depend to

a certain extent on the degree of contamination, on the degree of tissue injury and resultant necrosis, tissue tension, presence of blood, and other factors which may interfere with proper wound healing. The agents which are most frequently encountered are usually the staphylococci. Recently organisms such as the pseudomonas, proteus, and coliform bacilli have been encountered. On rare occasions one may encounter the hemolytic streptococcus. Unfortunately some of these such as the pseudomonas, the proteus, the coliform, and many strains of staphylococci are resistant. The hemolytic streptococcus usually is not resistant. The fact that most of these organisms are resistant to therapy once the infection has been established is an argument for the use of prophylactic agents. The difficulty of controlling an intraocular infection once it has started is a problem to everyone who has had to deal with this type of case. If it were possible to handle ocular infection satisfactorily once the infection had started, preoperative prophylactic therapy would not be required. If this were possible, the chance of superinfection due to micro-organisms that are drug-resistant and due to micro-organisms which flourish when the competitive bacterial flora is killed off by the prophylactic antibiotic selected would not occur. Unfortunately, such is not the case in ophthalmology, and one has to make a choice as to whether or not to use prophylactic therapy with the possible undesirable complications which can arise in such therapy or to risk the possibility of the development of an intraocular infection. It is quite true that intraocular infections are rare following ordinary elective intraocular surgery such as in glaucoma or following cataract extraction procedures. On the basis of this one may say that the risk of a patient developing a sensitivity to penicillin or an anaphylactic reaction to penicillin argues against the use of this drug. The risk of blood dyscrasias occurring following the use of chloramphenicol might prevent a physician from using this agent in prophylactic therapy of elective surgical cases. One cannot dogmatically state that such a feeling is incorrect. On the other hand, if one is dealing with a possibly contaminated eye such as after intraocular foreign body extraction or following a traumatic injury from an unclean object, prophylactic therapy would be advisable and justifiable, even in view of the possible complications of such therapy. One may argue that such prophylactic chemotherapy in a possibly contaminated case is acceptable on the basis that an infection is avoided and optimal wound healing obtained as the micro-organisms in the area of the ocular wound will be reduced to the lowest possible number. One would be justified in continuing such prophylactic therapy for two to three days. It is extremely difficult to evaluate properly antibiotic prophylaxis in clean intraocular surgical cases and even in those following trauma or foreign body penetration. One must keep in mind, on the other hand, as pointed out by Pulaski (1955), that the number of cases of superinfection, sensitization, untoward reactions are increasing as well as the number of resistant micro-organisms that have been encountered in hospital practice. It is necessary for the ophthalmic surgeon to evaluate each case carefully as to the value of prophylactic treatment and not to use a blanket rule for all cases. He should select the case which he feels prophylactic therapy is most

apt to benefit. This therapy should be employed only for a minimum length of time to be reasonably certain that he has overcome chances of contamination from surgical procedures.

ANTI-TUBERCULOUS AGENTS

It has been well established that for active tuberculous infections streptomycin and para-amino-salicylic acid in combination is an effective form of therapy. The isonicotinic acid hydrazides have also been shown to have high degrees of success as anti-tuberculous agents. It has been demonstrated that when locally or systemically administered, isonicotinic acid hydrazides and its isopropyl derivatives penetrate readily into the intraocular tissues and fluids (Kratka, 1955). From the experimental data in intraocular infections it is obvious that therapy must be continued for long periods of time in order to produce quiescence of the inflammatory tuberculous reaction. Even after four to six months of therapy an occasional eye will show a flare-up in inflammatory activity with cessation of therapy. With shorter therapeutic periods, i.e., less than two months, many recurrences of the inflammatory activity have been noted. This necessity for long-term therapy indicates that the agent has a bacteriostatic rather than bacteriocidal action. It is also apparent that tuberculous organisms will develop resistance to isonicotinic acid. There are reports in the literature of isoniazid being of help in leprosy and, *in vitro*, against certain fungi. There is evidence that the combination of streptomycin and isoniazid is more effective against tuberculous infection than either alone. This combination does not prevent completely the development of organisms resistant to streptomycin or to isoniazid. The combination of isoniazid and streptomycin is synergistic, not only in regard to the development of resistance but also in the more rapid destruction and inhibition of the organism. Isoniazid is not free of toxic effects. Although the reported incidence of toxic reaction is small, nevertheless there have been a few occasions of hemorrhagic episodes and gastrointestinal disturbances reported. Withdrawal symptoms may occur when the drug is stopped suddenly. Prolonged therapy may induce pyridoxine deficiency manifested by peripheral neuritis (Biehl and Vilter, 1954; Rosen, 1955). Patients have usually been carried on approximately 300 to 400 mgm. of isoniazid daily in combination with one gram of streptomycin every second or third day. Isoniazid may be administered orally, and these two agents can be employed along with para-amino-salicylic acid, 10 to 12 gm. daily. It is obvious that the use of streptomycin and isoniazid in ocular tuberculosis will be limited. The difficulty of diagnosing ocular tuberculosis is evident to all, and if one limits the use of these agents only to confirmed diagnoses, the number of patients with ocular disease treated with these drugs will be small (Knapp and Von Sallman, 1954; Woods, 1954; Kratka, 1955; Woods et al., 1954).

Role of Cortisone Combined with Antibiotics in Ocular Infection. Cortisone alters the inflammatory tissue response to bacteria and other infectious agents. This tends to reduce some of the natural defense mechanisms. The reduced inflammatory action lessens the natural protection against bacterial invasion.

These steroidal substances do not seem to reduce the effectiveness of antibiotics, when the organism is susceptible to the antibiotics. The question of the use of cortisone or ACTH or hydrocortisone along with antibiotics for the control of intraocular infections has not been answered. ACTH might prove useful as adjuvant therapy in the treatment of intraocular infection. It may reduce the severity of the inflammatory reaction while the antibiotic is successful in overcoming the growth and multiplication of the infecting agent. By reducing the inflammatory reaction the ACTH may reduce some of the tissue destruction and subsequent visual loss. Therefore, there may be a place for such steroidal therapy in the control of intraocular infection (Leopold, 1954). There is good evidence that virus infections are frequently accelerated by the use of these steroidal substances.

Other Chemotherapeutic Agents. Agents such as sodium proprionate have been shown to have some definite effectiveness in the control of external ocular infections. These compounds seem to work because of their ability to influence the carbohydrate metabolism of the organisms. Nitrofurazone (Furacin) has some antibacterial activity. It appears to act by interfering with the enzymes which contain sulfhydryl groups in susceptible bacteria. It seems to have been effective in some external ocular infections. Theodore (1955) has recently investigated another effective sulfonamide for local ocular use.

ANTI-INFLAMMATORY AGENTS

Mention should be made of Butazolidin or phenylbutazone. This compound was synthesized by Stenzl in Switzerland in 1948. It was given extensive trial in Europe, usually in combination with aminopyrine. In the United States most of the attention has been paid to the phenylbutazone component alone. It has been found that this compound when administered systemically affects the electrolyte balance. There is apparently a temporary decrease in urine volume, coupled with a significant retention of sodium and chlorine ions. There is also an influence on the blood, vascular and coagulation mechanisms, in that it will produce a significant drop in platelet count, mild anemia, unexplained hemorrhage, and occasional incidence of granulocytopenia. The compound possesses antipruritic, antihistaminic, and slight analgesic actions. It has the property of inhibiting the inflammatory action produced by artificial chemical or physical irritation in the experimental animal. It apparently gives relief in arthritis, but its analgesic action is not as great as that of salicylates although its anti-arthritic action appears to be greater. In many aspects it resembles the action of cortisone, suggesting that it might be a simple stimulant of the pituitary-adrenal action. However, there is no evidence that phenylbutazone affects urinary ketosteroid excretion, the eosinophil count or the insulin requirement in diabetes. This is definitely a toxic agent and should be employed only with a full awareness of this characteristic. It has had no fair trial alone in ophthalmology, but as Irgapyrin which is a mixture of amidopyrine and Butazoladin, it has received a fairly extensive trial on the European continent.

Yourish and his co-workers (1955) have demonstrated that phenylbutazone

(Butazolidin) administered intramuscularly is capable of blocking the inflammatory effects produced by glycerine injected into the anterior chamber of the rabbit's eye. Although he was unable to demonstrate the penetration of this material into the aqueous humor, Yourish believed that the anti-inflammatory effect is comparable to that obtained with cortisone. He was unable to demonstrate any local action of phenylbutazolidine when applied as an ointment.

STEROIDS

The use of local and systemic steroids has become commonplace in ocular therapy. The addition of cortisone, hydrocortisone, and ACTH to the therapy of ocular inflammation and allergies has added considerably to the ophthalmologist's ability to influence the course of these diseases.

Topical steroid therapy has been employed for conditions such as conjunctivitis of vernal, allergic, and chemical origin, and even bacterial when the steroid is able to be combined with the proper antibiotic. In similar fashion it can be used for corneal diseases. Not all corneal diseases respond to local steroids. These compounds appear to be contraindicated in epidemic keratoconjunctivitis and in acute herpes simplex keratitis. Local therapy has often proved efficient in anterior uveitis. Most intraocular lesions respond to systemically administered steroids in a fashion superior to local administration.

Uveitis of unknown etiology including sympathetic ophthalmia and ophthalmitis phakoanaphylactica, respond to systemic therapy with agents such as hydrocortisone and ACTH. It is well known that hydrocortisone can be given orally, intramuscularly, or intravenously. ACTH may be given intramuscularly or intravenously. A variety of retinal, choroidal, and optic nerve disorders may respond to the systemic route of administration.

There does not appear to be any advantage to retrobulbar injections of steroids, but subconjunctival administration appears to produce a beneficial effect occasionally greater than that obtained by topical administration.

New Steroid Derivatives. It is now approximately seven years since cortisone was first used in the therapy of ocular disease. Since that time several closely related compounds have been prepared and many tried in ophthalmology. Hydrocortisone, hydrocortisone-T-butyl acetate, a higher ester of hydrocortisone, 9-alpha-fluorohydrocortisone, Meticorten, and Meticortelone are examples.

Hydorcortisone-T-butyl-acetate appears to offer no advantage over hydrocortisone acetate in ocular disease.

9-Alpha-fluorhydrocortisone acetate or 9-alpha-chlorohydrocortisone acetate has been found to exert an anti-inflammatory effect greater than cortisone acetate or hydrocortisone acetate when compared in equal concentrations. In some experiments the effect was ten times as great. However, the systemic use of these new agents is limited by their salt-retaining effect which produced more edema than encountered with earlier use of cortisone and hydrocortisone. The chief value of 9-alpha-fluorhydrocortisone would appear to lie in its local application.

Meticorten, prednisone, or Δ-1-dehydrocortisone and Meticortelone and prednisolone or Δ-1-dehydrohydrocortisone appear approximately four to five times

as potent as cortisone in their anti-inflammatory effect in rheumatoid arthritis. The data available on their activity in ocular disease suggests that these agents are effective. They also appear to be effective in four to five times lesser concentration than that required for cortisone and hydrocortisone. Occasionally they are successful antiphlogistic agents in ocular diseases which have not yet responded to doses of the earlier steroids. Usually, however, they produce the same effect but smaller doses are required to bring about this action. The salt-retention and potassium nitrogen loss seen with cortisone administration are apparently minimized with the action of these new steroids.

The chief agents which are now employed for local use are hydrocortisone acetate and free alcohol, prednisolone acetate or free alcohol, prednisone acetate and free alcohol, and 9-alpha-fluorohydrocortisone acetate or free alcohol. For systemic usage Meticortone, Meticortelone, or prednisone or prednisolone, or Δ-1-dehydrocortisone or Δ-1-dehydrohydrocortisone are being used in preference to the earlier cortisone and hydrocortisone. Time will be required to evaluate properly these newer steroid derivatives in comparison with the older ones (King and Weimer, 1955).

AUTONOMIC DRUGS

The most useful classification of autonomic drugs employed in ophthalmology is based on the neurohumoral theory of nerve impulse transmission (Leopold, 1955). The theory states that impulses are transferred from nerve fiber to nerve cell and from the nerve-ending to the affector organ by the mediation and liberation of a chemical substance. Acetylcholine is the neurohormone which is thought to be responsible for the activation at the ending of parasympathetic nerve fibers, for transmission at the sympathetic and parasympathetic ganglia, across synapses of the central nervous system, and activation of the structures innervated by spinal nerves such as skeletal muscle. These activities can be further divided into muscarinic and nicotinic effects. The muscarinic effect is used to describe the stimulation which occurs at the endings of the parasympathetic postganglionic nerve fibers, and the nicotinic action is that which occurs at the autonomic ganglion or myoneural junction.

The adrenergic nerve mediator is possibly l-arterenole (norepinephrine). This is thought to be the substance formed at the postganglionic endings of the sympathetic nervous system. Other substances which may be formed are epinephrine, tyramine, and hydroxytyramine. The last two substances have a very weak sympathomimetic action. The term sympathin may be used to define the group of substances which may be liberated following adrenergic nerve stimulation. After stimulation of the cervical sympathetic nerve fibers arising from the superior cervical ganglion, the sympathomimetic activity in the aqueous humor is said to be increased. The relative amounts of epinephrine and arterenole vary. Epinephrine usually predominates and it is a more potent iris dilator than neo-epinephrin or norepinephrine in normal aqueous humor of experimental normal eyes. They did find arterenole in the iris and ciliary body.

The classification of autonomic drugs employed in ophthalmology, using the neural humoral theory, can be seen in Table 1.

TABLE 1

Classification of Autonomic Drugs

I. Drugs Acting on Parasympathetic System (Parasympathomimetic)

A. Drugs acting on effector cells so as to mimic action of acetylcholine, or the so-called neurohumoral transmitter

1. Pilocarpine
2. Carbacol U.S.P. (doryl)
3. Furtrethenium iodide (furmethide iodide)
4. Methacholine chloride U.S.P. (mecholyl chloride)

B. Inhibitors of enzyme cholinesterase, which normally hydrolyzes neurohumoral transmitting agent, acetylcholine (the action of the locally produced acetylcholine (the action of the locally produced acetylcholine is therefore markedly prolonged)

1. Physostigmine (tertiary compound with a urethan group)
2. Neostigmine (prostigmin), quaternary compound with a urethan group
3. Diisopropylfluorophosphate
4. Tetraethylpyrophosphate
5. Hexaethyltetraphosphate
6. Mintacol

C. Drugs producing varying degrees of paralysis of effector cells to impulses from parasympathetic postganglionic nerves or to stimulation by drugs like pilocarpine. (These paralyzing drugs prevent access of acetylcholine or stimulating drug to the irritable patches of the surface of effector cells)

Visceral and Intraocular Structures	Skeletal Muscle
1. Atropine	1. Curare
2. Homatropine	2. Tubocurarine chloride
3. Eucatropine U.S.P. (euphthaline)	3. Decamethonium iodide
4. Scopolamine	
5. Hyoscyamine ("Duboisine")	
6. Dibutoline	
7. Banthine	

II. Drugs Acting as Sympathomimetic Agents

A. Drugs acting on effector cells so as to mimic action of the neurohumoral transmitter, probably epinephrine, sympathin E, or arterenol.

1. Epinephrine
2. Phenylephrine (neo-synephrine) hydrochloride
3. Hydroxyamphetamine (paredrine)
4. Ephedrine
5. Amphetamine (benzedrine)

(2–5: Phenylalkylamine derivatives)

B. Enzyme inhibitors preventing destruction of epinephrine, which is essential for neurohumoral transmission in the sympathetic nerve endings. (The locally produced epinephrine thus has a prolonged effect. This anti-epinephrine substance may be an amine oxidase.)

1. Cocaine (?)
2. Ephedrine (?)
3. Amphetamine (?)
4. Procaine (?)

C. Adrenergic-blocking agents—compounds that specifically inhibit certain responses of effector cells to epinephrine, related amines, and sympathetic-nerve impulses.

1. Beta-halo-alkylamines, e.g., Dibenamine (N-N-dibenzyl-B-chloro-ethylamine hydrochloride)
2. Imidazolines, e.g., benzazoline (Priscol)

TABLE 1—*Continued*

3. Benzodioxanes, e.g., 993 F
4. Ergot alkaloids, e.g., dihydroergocornine
5. Yohimbines

III. Ganglion-Blocking Agents
- A. Agents interfering with transmission through ganglia, similar to secondary effects (paralyzing) of nicotine (large doses)
  1. Tetraethylammonium chloride (Etamon Chloride)
  2. Pentamethonium iodide
  3. Hexamethonium iodide

IV. Centrally Acting Agents
- A. Drugs influencing centers in brain, e.g., medulla and diencephalon, that are superimposed over the connector cells of the autonomic system
  1. Hypothalamic center responds to cholinergic agents, e.g., acetylcholine; physostigmine, etc., can produce parasympathetic or sympathetic activity, depending on area of hypothalamus stimulated; e.g., stimulation of preoptic region gives parasympathetic response; postchiasmal area, sympathetic response
  2. Cerebral cortex also responds to acetylcholine and physostigmine
  3. Other agents or conditions that act centrally are morphine, CO_2 and oxygen lack

V. Directing Agents
1. Histamine
2. Barium, potassium, etc.
3. Procaine (?)
4. Ergot alkaloids, benzodioxanes

Anticholinesterase. There are two types of choline esterase. One of them, the acetylcholinesterase, specific cholinesterase or true cholinesterase, is present in high concentration in all nervous tissues, human erythrocytes, and hydrolyzes acetylcholine rapidly. The other is known as the nonspecific cholinesterase or pseudocholinesterase, and it tends to split long-chain cholinesters at a greater velocity than it does acetylcholine. The cholinesterase found in ocular structures, including iris, sphincter ciliary muscle, is predominantly the specific type. De Roetth has demonstrated that the cholinesterase content of the iris drops to about 40 per cent of its former level following ciliary ganglionectomy. The anticholinesterases may be divided into three groups: (1) physostigmine and other urethanes; (2) the quaternary ammonium bases (neostigmine methylene blue); and (3) organophosphorus compounds. These inhibitors may be further classified, by virtue of their duration of action, into those which inhibit cholinesterase reversibly, and those which produce an irreversible inactivation of cholinesterase. Physostigmine and neostigmine are examples of reversible inhibition, and diisopropylfluorophosphate, of irreversible activity (see Table 2).

Amine-Oxidase. There is an enzyme in the sympathetic system which inactivates sympathins. It has been demonstrated to be present in the iris and mictitating membrane of experimental animals. Amine-oxidase has the property of destroying arterenole more rapidly than epinephrine, and after denervation of the iris, the enzyme activity in the iris is reduced. Cocaine and ephedrine are thought to act at least partially by their ability to inhibit the activity of amine-oxidase.

TABLE 2

Variations in Effect of Anticholinesterase Agents

	Neostigmine	Physostigmine	Diisopropyl Fluorophosphate (D.F.P.)
Ability to unite with cholinesterase	Short, reversible union	Longer, reversible union	Longest, irreversible union
Myasthenia gravis	Most pronounced improvement, short duration	Small improvement, short duration	Small improvement, long duration
Effect on central nervous system	Depression	Excitation	Excitation
Lipid solubility	Insoluble	Soluble	Soluble
Combined effect on pupil	Blocks D.F.P.; not blocked by D.F.P.	Blocks D.F.P.; not blocked by D.F.P.	Blocked by physostigmine, and neostigmine; does not block neostigmine or physostigmine

Cholinergic Blocking Agents. Cholinergic blocking agents comprise a variety of substances that have in common the property of interfering with acetylcholine or of drugs that act like acetylcholine. These blocking substances probably act by virtue of structural similarity at least in part to that of acetylcholine. Since acetylcholine acts at effector organs, such as the sphincter of the iris, at ganglia such as the ciliary ganglion in the central nervous system, and at the effector organs such as skeletal muscles, there are cholinergic blocking agents that can act at each or all of these sites. Most of the cholinergic blocking agents have one site at which they are most effective. Atropine and related substances are capable of blocking all actions to some degree but are used primarily to block the peripheral parasympathetic actions. This can be brought about with lower dosage than required to produce blocks in other sites. There are other agents that produce central nervous system and ganglion blocks to a greater degree than they produce peripheral blockade. The control of central actions with a minimum of peripheral effect can be accomplished with a number of compounds such as Diparcol, Parpanit, and even a few of the antihistaminics such as Benadryl and Dramamine. These drugs are all in current use to reduce the spasticity of Parkinsonism.

Peripheral Parasympathetic Blocking Agents. These agents block response of the effector cells to the direct acting drugs and to nerve stimulation. Most of these have been employed in ophthalmology as agents to produce cycloplegia and iridoplegia. Many of these compounds have been investigated in ophthalmology. Swan (1949) introduced dibutoline sulfate and several British investigators studied a compound called E-3 or lachesine. Many of these peripheral cholinergic blocking agents have their greatest action on the gastrointestinal tract. Examples are agents such as Bentyl (dicyclomine) and Prantyl (diphenmethanil methylsulfate). Their ocular action is weak.

Ganglion Blocking Agents. Ganglion blocking drugs interfere with the transmission of impulses at both parasympathetic and sympathetic ganglia. Most of

these compounds are quaternary ammonium bases. Some of these quaternary compounds have their greatest activity at the ganglion. Others interfere with activity at the neuromuscular junction. Pentamethonium and hexamethonium iodide are potent ganglion blocking agents, whereas decamethonium iodide blocks the myoneural junction safely. Hexamethonium iodide has been used widely for therapy of systemic hypertension. It has a predominant effect on the sympathetic ganglia and causes a fall in blood pressure. However, this compound also blocks parasympathetic ganglia, and so may produce some undesirable aspects when used in high concentration in the therapy of systemic hypertension. Some of these agents, such as pentamethonium iodide and hexamethonium iodide may cause dilatation of the pupil, relaxation of accommodation and may actually bring about a slight decrease in intraocular pressure.

Neuromuscular Blocking Agents. The neuromuscular blocking agents which have curare-like action have received some attention in ophthalmology. Two types of compounds may be identified. There are those agents that appear to interfere with the action of acetylcholine on the motor end plate, probably by a simple substrate competitive type of mechanism. These compounds may also interfere with the formation of acetylcholine at the myoneural junction. This type of activity demonstrated by Tubo-curarine USP, is a true curariform agent. Its activity can be overcome by neostigmine. The other group of curare-like agents seems to act as though there were an excess of acetylcholine, which would depolarize the muscle as well as the motor end plate. Decamethonium acts in this method. Its activity is not overcome by neostigmine. Succinylcholine chloride acts like decamethonium, but it seems to be overcome by cholinesterases, and its action therefore is very short. It also produces paralysis quickly. Because of the rapid onset and short length of activity it can be used without too much danger. Nevertheless, none of these neuromuscular blocking agents should be employed without a thorough knowledge of their activity and readily available methods of overcoming an undesirable response.

Adrenergic or Sympathetic Blocking Agents. An adrenergic blocking agent blocks the effect of epinephrine on the effector cell. Sympathetic blocking agents or sympatholytic agents are terms which are reserved to describe those agents which block the response to stimulation of the sympathetic nerves. Several of these agents, particularly dibenamine, have had trials in ophthalmology for the control of glaucoma. These are of some value in the treatment of acute narrow-angle glaucoma which has failed to respond to other therapy. It is possible that these agents are interfering with the formation of aqueous humor although the evidence is not complete. These agents are employed for the diagnosis of pheochromocytoma, for the therapy of various peripheral vascular diseases and have been tried in systemic hypertension.

Combinations of Autonomic Drugs. There are theoretical reasons why certain autonomic drugs in combination should be more effective than either agent alone. The combination of epinephrine along with cocaine produces greater dilatation than either agent alone. It may be that cocaine is blocking the destructive action of aminoxidase on epinephrine. However, as pointed out by

Leopold and MacDonald (1948), the combination of certain agents may reduce the effectiveness. Physostigmine will block the activity of diisopropylfluorophosphate. On the other hand, if diisopropylfluorophosphate is instilled prior to physostigmine, a combined activity is obtained. Thus not only are the activities of combinations to be considered, but also the time sequence of instillation. Recently Swan and Gehrsitz (1951) have indicated that the combination of pilocarpine with physostigmine may reduce some of the ocular activity of physostigmine. Instead of a synergistic or additive action being obtained, the weaker miotic may reduce the effectiveness of a stronger drug. These observers felt that pilocarpine decreased the reactivity of the iris sphincter of the albino rabbit to physostigmine and diisopropylfluorophosphate as well as to physiologically produced acetylcholine. Lowenstein and Loewenfeld (1953), on the other hand, were unable to demonstrate that pilocarpine could inhibit the effect of physiologically produced acetylcholine on the normal human pupil. They found that the combined administration of small doses of pilocarpine and physostigmine was generally more effective than the instillation of either drug alone, and concluded that the combined effect on the pupil was additive and not competitive.

ANTIHYPERTENSIVE DRUGS

Great interest has been shown in many compounds which have been employed for the therapy of systemic hypertension: such drugs are hydralazine and the alkaloids of rauwolfia serpentina, particularly reserpine. The exact site of action of many of these drugs is not known. Some of them are thought to act on the higher nerve centers such as the hypothalamus or even the cortex. Others are thought to act on the barocepters of the aortic arch and carotid sinus.

Drugs such as reserpine have a definite tranquilizing and sedative effect on the patient. Usually these drugs are used in combination, i.e., ones which are thought to act on the neurogenic element, on the higher centers, are combined with ganglionic blocking agents (Harris, 1955).

It has been suggested by Thiel (1954) that such compounds may have some value as adjuvant therapy in glaucoma.

It is well to realize that all of these compounds have serious side effects. Rauwolfia serpentina alkaloids, for example, produce serious mental depression at times. Some of them also produce nasal congestion, shortness of breath, weakness, bizarre dreams, gastrointestinal disturbances. Some of them produce miosis. Hydralazines have been known to produce some collagen-like disorders, particularly resembling lupus erythematosis (Freis, 1954; Reinhardt and Waldron, 1954). Bruce (1955) has called the attention of the ophthalmologist to a patient with essential hypertension who four minutes after being given hexamethoniumchloride intramuscularly began to notice failure of vision and a few minutes later became totally and permanently blind.

Antihistaminics and Clinically Related Agents. The use of antihistaminics in ophthalmology is gradually diminishing, but a drug related to the antihistaminics, namely, chlorpromazine, has received a great deal of attention in other branches of medicine. It has a very slight effect as an antihistaminic but has

marked action in controlling postoperative nausea and vomiting and in hiccoughs. It appears to enhance the analgesic effect of opiates and the action of sedatives. It has been suggested that it may have some value in the therapy of acute glaucoma and others have considered its use for the preoperative and postoperative ophthalmic patient.

The drug may be used in dosage up to 50 mgm. orally in a single dose or in divided doses of 25 to 50 mgm. four times a day. It may also be used intramuscularly up to 25 mgm. The drug produces marked hypotension and drowsiness so that the patient sometimes appears almost moribund. Occasional instances of jaundice resembling the obstructive type have been reported. An elevation of the serum alkaline phosphatase is one of the earliest signs of hepatic impairment. The condition is reversible if the drug is discontinued. A few patients have had allergic skin reactions. Some patients complain of dryness of the mouth and nasopharyngeal mucosa. The drug should not be given to any patients who have taken large quantities of sedatives or alcohol because of its potentiating effect and should not be given to any patients with liver damage.

FEVER THERAPY

There is considerable evidence that the favorable response following the use of foreign protein therapy in ocular therapeutics may be due to stimulation of the adrenal cortical mechanism; however, there are differences. In rabbits, the Arthus phenomenon as elicited by crystalline egg albumin is inhibited by cortisone, but it is enhanced by pyromen (Stuart, 1951). Newell (1951) has indicated that the occasional prompt beneficial effect of pyromen when corticotropin and cortisone have failed may be due to important actions other than the adrenocortical stimulation. Some of the beneficial effects of tissue therapy may also fall into this group of agents which are responsible for either stimulating the adrenocortical mechanisms or by supplying some hormonal substance. The present status of tissue therapy in ophthalmology is quite uncertain.

RADIOACTIVE ISOTOPES

Within recent years physicists have placed a most powerful tool, the radioactive isotope, in the hands of the biologists. There are some who believe that this tracing method of investigation will prove in the long run to be the most fruitful physical technique yet adapted to biological investigation. Radioactive material has been used for the making of radio-autographs. This consists in placing organisms or histologic sections containing radioactive isotopes adjacent to a photographic emulsion, and recording in the reduced metallic silver of the emulsion an image of the radioactive areas of the object. This is possible because of the faculty of the alpha particles, beta particles or gamma rays given off by the isotopes to reduce photographic emulsion in a manner similar to light. The radioactive isotopes have been used in the study of thyroid metabolism in estimation of volume of body fluids, in the therapy of thyroid disease, in the treatment of blood disorders, and, most recently, in the localization of tumors. Radioactive phosphorus has received considerable attention during the past few years

in the localization of intracranial neoplasm. Recently this substance has been investigated for its value in localizing intraocular tumors. A number of independent investigators including Thomas and his co-workers (1954), Dunphy and his co-workers (1953), Eisenberg and his co-workers (1954), have reached the fairly uniform conclusions that gamma emitters are not satisfactory for this study and that beta emitters do have possible value in this regard. At the present time, radioactive phosphorus appears to be potentially valuable as an aid in differential diagnosis of intraocular tumors, but does not supplant older time-tested methods.

Beta-Irridation. Hughes (1952) has summarized the work with beta irradiation and has pointed out that this may be used effectively in a variety of ocular conditions consisting of epithelial tumors of the limbus and cornea, vernal catarrh, rosacea keratitis, primary vascularizing keratitis, recurrent pteregium and vascularization complicating keratectomy, and keratoplasty. It may be also helpful in phlyctenular keratoconjunctivitis, a variety of inflammatory infiltrates in the cornea, nodular episcleritis, and to reduce granulation tissues. There are many undesirable reactions after beta radiation. There is frequently immediate and delayed irritation following application of the beta irradiation. Postradiational vessels may form, loss of lashes may occur; there may be late corneal ulceration, and there may even be a rise in intraocular pressure in those eyes which have had large total doses of beta exposure. There is always the danger of cataract formation, particularly when large doses of beta irradiation have been employed. This technique in therapy should only be employed when it is thought to be superior to other forms of treatment. It should only be used by someone well versed in the difficulties of standardizing technique and with all its contraindications.

ANTICOAGULANTS

Blood Coagulation. Under normal conditions the circulating blood is maintained in the fluid state by a complex and not yet fully understood balance of clotting and anticlotting forces. Some circumstance may disturb the balance; i.e. injury of the vessel wall, slowing of the circulation, stress of a general systemic operation, some inflammatory infectious focus in the body, alterations in the blood elements themselves, etc.

It has been established for some time that both heparin and coumarin derivatives reduce further formation, and propagation of the intervascular clotting. Several recent reports indicate that these agents under experimental conditions also facilitate the reopening and recannulization of established acute thromboses in arteries and veins. Heparin was the first that was discovered of the presently employed anticoagulants. It is expensive but has an excellent and immediately effective antidote in protamine sulfate. It should be controlled in its administration by the venous clotting time using the method of Lee-White. The coumarin indanedione compounds are agents which produce an anticoagulant effect, principally by inducing a moderate degree of hypoprothrombinemia. In addition, however, they also decrease the agglutin ability and adhesiveness of platelets. They

have the advantage over heparin in that they are less expensive. In addition to the hemorrhagic dangers similar to those of heparin, these agents also vary in the amount required in the individual patients to bring about the desired effect, and the patient's prothrombin time must be analyzed at very frequent intervals to determine how much should be employed.

Anticoagulants have been employed in ophthalmology in the hope of successfully attacking the problem of thrombosis of the central retinal vein or its branches. The use of anticoagulants has been established as the treatment of choice in the great majority of cases of thrombophlebitis with or without embolic episodes elsewhere in the body. However, considerable question still remains concerning their value in ophthalmology. The evidence is not conclusive in regard to central vein closures. There is some indication that the use of anticoagulants reduces the incidence of the complications of hemorrhagic glaucoma (Duff, Falls and Linman, 1951) and may result in some increase in subsequent visual acuity (Maumenee, 1953). Klien has stressed the importance of the prophylactic use of these agents in ophthalmology. There is no doubt that there have been many failures with the anticoagulants. There have been patients that have developed thromboembolic complications despite the maintenance of so-called therapeutic levels of clotting and of prothrombin time. Uniform responses to a given dose cannot be obtained in all patients and the use of these anticoagulants is accompanied by certain definite risk of hemorrhage. The successful attack on thrombosis requires prevention of the original development, or multiplication of any already formed thrombi, the prevention of the delivery of emboli from the thrombus and the encouragement of the breaking up of the original thrombus. Their use requires a physician who is fully cognizant of all the dangers and the proper means to employ them and accurate technicians. The agents which are available for use in ophthalmology are heparin, dicumarol, Tromexan, paritol, phenylindanedione and 4-hydroxycumarin No. 63 (Link).

Experience with tromexan 3,3-carboxymethylene (4-hydroxycumarin) demonstrated that in the majority of patients following the administration of 1500 to 1800 mgm. the drop in prothrombin is more rapid than following the administration of dicumarol. However, the rate of action varies individually. Some patients show a resistance to Tromexan as they did to dicumarol, and a patient may be stabilized and then suddenly show a lack of control. This is somewhat more common with Tromexan than with dicumarol. If there is a sudden rise of prothrombin time of sixty or more seconds, usually the omission of one or two doses will return the prothrombin to a safe level within 24 to 36 hours. Most patients, following an initial dose of 1500 to 1800 mgm. are controlled with a dosage of 300 mgm. two or three times a day. Tromexan seems to be about one-fifth as active as dicumarol. Because of the rapid ability of the prothrombin level to return toward normal with Tromexan administration, vitamin K or transfusions are rarely required.

There is evidence that the use of cumarin derivatives such as Tromexan do exert a definite effect on a thrombus which is already formed. This clearing is thought to be due to fibrinolysin and other enzymes in the blood which act with

greater effectiveness when the clot forming elements of the blood are rendered less effective by the presence of anticoagulants.

Phenylindandione appears to have a more prompt action on prothrombin than that of dicumarol. Vitamin K does not appear to be effective in counteracting the action of phenylindanedione. There are a number of patients who have a resistance to phenylindanedione, and it is somewhat harder to control than that of dicumarol or Tromexan. Nevertheless, bleeding has been rare with its use. Because of the difficulty of control, the lack of predictability in its action and the fact that it cannot be counteracted by use of vitamin K it is theoretically a less desirable drug than either Tromexan or dicumarol.

Cyclocumarol (4-4-hydroxycumarin anticoagulant No. 63 B-L-5) is another antiprothrombin agent. A single dose of 2 mg. per kg. appears to produce a satisfactory prothrombin time within 24 to 48 hours, somewhat more rapid than that seen with dicumarol but its action is much more prolonged. In some instances the prothrombin effect will be in existence from four to fourteen days following the initial dose. Therapeutic levels have been obtained on dosages administered every two to five days. It can be overcome, not by a water soluble vitamin K but by vitamin K_1 in dosage of 250 to 500 mgm. given orally or parenterally. Cyclocumarol appears to be two to three times more potent per unit of weight than dicumarol, and ten to fifteen times more potent than Tromexan.

Paritol, a synthetic polysulfuric acid ester of polyanhydromannuronic acid, is similar to heparin in both chemical structure and action. As compared with heparin, it is about one-seventh as active but it has certain toxic features at the present time which preclude its widespread use. Treburon, a polyhexuronic derivative has anticoagulant properties similar to heparin. It is about one-third as potent as heparin. At the present it is being investigated clinically for a short term, or the initial stages, of anticoagulant therapy.

A lipid thromboplastic inhibitor, perhaps antithromboplastin, the inositol phosphatide fractions of rabbit brain and lung, of soy bean and of plasma phosphatides have been found to contain an active component which may be an antithromboplastin. This lipid inhibitor may have an important role in anticoagulant therapy. Further studies will determine its exact value.

There is some interest in dl-alpha-tocopherol derivatives as anticoagulant substances. Most of the evidence does not show any significant effect of these derivatives in the prevention or treatment of thrombo-embolic conditions.

Antibiotics such as chloramphenicol, Terramycin or aureomycin decrease the amount of dicumarol or anticoagulant drug required. They may be doing this through their interference with the bacterial flora of the intestinal tract. Since the production of vitamin K is largely dependent on the action of the bacterial flora, these antibiotics may be interfering with this production. One should be cautious when using anticoagulants and antibiotics simultaneously.

There is some insecure evidence that ACTH and cortisone may shorten the coagulation time (Wright, 1952; and Lyons, 1955).

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Clinical Practice

ACCOMMODATION AND REFRACTION

MEASUREMENTS OF VISUAL ACUITY

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Brit. J. Ophth., 1955, *39:* 513–533

Visual acuity is a measure of the eye's ability to discriminate detail. It is expressed as the reciprocal of the angular subtense, in minutes of arc, of the separation that can just be detected between two objects. The ability to detect detail depends upon the nature of the object and upon the eye. Visual acuity also depends upon the criterion for successful detection that is used. Of these three factors, the nature of the detail (including the method of presentation) as well as the criterion for detection can be completely determined by the experimenter. The eye, however, forms part of a complex nervous system and the subjective image is affected by many physical and mental factors. Some of these are understood and may be kept constant during an experiment, but the majority are fluctuating continuously and large variations in visual acuity occur in any observer. Hence, any measured visual acuity is only true for the instant of measurement; consequently many observations must be made to obtain a useful average result.

The test object usually consists of some fine detail which has to be discovered with respect to an easily seen reference object. Many test objects have been devised, the most common being the Landolt broken circle, parallel bar gratings, and the Snellen test chart. In the first series of experiments, a dark Landolt broken circle on a light background was employed; in experiments with color contrast, a colored test object and surround were used. A relatively high contrast between the test object and its immediate background does not cause a variation in visual acuity. In general, there appears to be little difference between colored and white backgrounds of equal luminance. A colored test object viewed on a colored background presents a color contrast as well as a luminance contrast, and as so many visual tasks in practice involve colored surfaces, it is surprising that little is known about these conditions. Movement of the test object greatly affects detection of its detail. A low velocity may improve the subject's performance, but as the velocity is increased the detail is soon rendered indistinguishable.

The criterion for assuming that the observer can perceive the detail presented will considerably modify the visual acuity presented to him. The standard of performance needed in most practical work is that the detail should be detected every time. However, as soon as the observer's performance rises above that due to chance, he is in fact detecting detail to some extent. The conditions required to attain 100 per cent perfection differ widely from those needed for a performance just a little better than that which may be achieved by chance.

The eye and brain and the nervous connections between them cannot be held constant; their performance will vary from moment to moment and day to day so that an observer, presented with a given visual task on different occasions, will give responses which vary, depending upon the observer and the severity of the task. Some observers are more than usually consistent in this type of experiment and it is more convenient to use a small group of such consistent observers than a large group of less consistent observers. The distance between observer and test object also has some effect upon the acuity of the observer. An alteration in the distance of the test object does not bring about an exactly corresponding change in the retinal image, because the posterior nodal distance of the eye alters during accommodation and increases the size of the image on the retina as the test object is brought closer to the eye.

In this study the image was projected onto a translucent screen and a spot light was used to illuminate the surround. Observations of the position of a Landolt broken circle were made at a distance of 1 meter.

At low luminance the size of the surround does not affect visual acuity. As luminance increases, an increase in size of the surround yields better visual acuity but further extension has progressively less effect. A considerable improvement follows an increase of the surround from 0.5 to 6°, but no significant change results from using much larger surrounds of 38 and 120°.

By increasing the luminance of the background to the test object, large increases in visual acuity are obtained up to the region of 100 ft. L. Beyond this luminance, visual acuity tends to remain constant and a maximum is obtained at a high luminance level the exact value of which depends upon surround conditions. At luminances above 1000 ft. L., which are only encountered in bright sunlight and on surfaces of lighting fittings, there is an overall reduction in visual acuity for all surround conditions.

Tests using colored Landolt broken circles were complicated by difficulties in observation arising from changes in apparent brightness of the test object with changes in size.

Comment: In this paper the authors are not concerned with visual difficulties stemming from refractive errors or pathologic states, but with average variations in visual acuity which result from changes in the luminance of test objects and their backgrounds. They consider not only the luminance level but also contrast, the latter studied by the use of colored objects and backgrounds as well as by the usual black on white.

Observers were selected on the basis of consistency of trial results and were required to have essentially normal visual acuity. The experimenters were fully aware of the varia-

tions which are to be expected in any series of subjective tests, especially in the series in which the colored test objects and surround were used.

Adaptation to the different levels of luminance was encouraged in order to rule out the marked differences in performance which would normally occur with an eye not adapted for the given level of illumination. With the Landolt broken circle as the object, so arranged that it could subtend ⅕ to 2 mm. of arc at the test distance, some 130,000 observations were made.

The results agreed very well with those of Luckiesh and Moss, which were reported from the NELA Park Laboratories in Cleveland during the early 1930's. Visual acuity was shown to increase rapidly with an increase in luminance (recorded in ft. lamberts) from a low of 0.1 ft./L., at which level less than 20 per cent of observations were correct, to 1000 ft./L., where the performance was nearly 100 per cent, this varying somewhat, but not greatly, with the size and luminance of the surround (background).

Above 1000 ft./L. the visual performance was not materially increased and in most cases lessened. Colored objects with contrasting surrounds gave less significant results, as might be expected, not only because of the impossibility of getting pure colors and matching luminance of the object and background, but also because of the usual variable sensitivity in a group of individuals to brightness levels in color.

From the ophthalmologic standpoint, the principal value of these carefully conducted experiments is to again emphasize that adequate illumination, both direct and reflected, contributes materially to normal performance.

Black on white test objects in the refraction room, in order to have consistent results comparable with those obtained from different types of objects, should have a brightness of at least 10 ft./L. or more with a wide surround.

Test objects in the refracting room should, in view of the results of these experiments, have a sufficiently high luminance to insure maximum visual acuity with proper correcting lenses, especially if the visual tests with one type of acuity chart are to be compared with those found with some other type.

Also of importance would seem to be the size of background and probably the spacing of the characters on the test chart. The surround, meaning the illuminated area surrounding a given character, should subtend at least 6° from the position of the patient.

The recommended levels of luminance seem rather high, thus suggesting that those which are now in general use are on the low side.

Practically, this problem can be solved for the refractionist if he will experiment with the illumination of his test chart, increasing it to the level at which no improvement in visual acuity occurs with greater illumination.

EDWIN F. TAIT

REFINEMENT OF CHECKERBOARD TARGETS FOR MEASUREMENT OF VISUAL ACUITY LIMENS

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J. Optical Soc. Am., 1955, *45:* 834–838

The determination of very small deviations in visual acuity necessitates measures of greater precision than are ordinarily used in testing. The checkerboard target is composed of one black and white checkerboard and three squares of the same size, formed by rows of closely spaced dots. Identification of the checkerboard from among the four squares is the test of visual acuity. When the angular size is too small to permit checkerboard resolution, the ideal appearance of the target is four uniform gray squares. Unfortunately, the latter condition is only infrequently achieved. Despite rigorous and painstaking application of current reproduction techniques, apparent differences in brightness and contour give secondary cues which confound the acuity task.

Substitution of a black background for the usual white surround eliminated secondary cues and accurate visual acuity measurements were obtained. Using targets at distances between 13.5 and 20.5 ft., the targets were presented at one-half ft. intervals and the per cent seen plotted for each reciprocal visual angle. A variation in target distance of 2.5 ft. in target size of 0.3 mm. produced a change in "per cent seen" from 100 to 0. This range is an approximate visual angle of 12 seconds. Under the conditions of the experiment, the interchangeability of varying the visual angle (1) by changing target size and (2) by changing target distance was established. In considering the results, data collected at 13.5 to 20.5 ft. may not be compared legitimately with data at 35 to 38.5 ft. except to note the limitation in varying size and distance concomitantly over large ranges.

Comment: We have the word of the Adjutant General's office proclaiming that the checkerboard target is the purest measure of retinal resolution. The authors have further improved on the usability of this type target. The clinician is glad to find from the authors' study that the accuracy of visual acuity testing is equal whether the target size or the target distance were changed during the tests, or not. It is interesting to note that a change of 12 seconds in visual angle increases the recognizability of target from 0 to 100 per cent. One wonders why it should be more "scientific" to express visual acuity data in reciprocal visual angle rather than in plain visual angle.

Arthur Linksz

THE STIMULUS TO ACCOMODATION

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Am. J. Optom. and Arch. Am. Acad. Optom., 1955, *32:* 422–431

This study was undertaken to determine if accommodation was voluntary or whether it was reflex in nature. Fincham (J. Physiol., 1953, *121:* 570–580) recently presented data which suggested that accommodation is a reflex triggered principally by chromatic aberration and the Stiles-Crawford effect.

The basic instrument used was the haploscope with targets presented to the right eye only. The targets were identical except that varying amounts of accommodation were required to see them clearly. The stimuli used varied from zero dropters to two dropters, to four diopters. Accommodation was recorded photographically by means of a camera which registered the reflected image from the lens. Convergence was measured by means of photography of the corneal reflex. An accommodation calibration curve was prepared by photographing the image from the front surface of the lens while the subject was accommodating a predetermined amount.

In one series of ten experiments the accommodation was consistently in the direction to yield a clear image suggesting the correctness of Fincham's theory. In two of twelve other experiments, however, the subject accommodated when relaxation was indicated. (This accommodation was inferred from the convergence records, the photographs of the anterior lens image being unsuitable.) The occurrence of the wrong response suggests to the author that accommodation is not controlled reflexly.

Further support of the voluntary control of accommodation was observed in the reaction times. All of the correct reaction times averaged 0.343 seconds. Correction of a faulty response, however, took 0.621 seconds. If the accommodative response were reflex, correction should occur within 0.34 seconds. On the basis of this experiment it was thus impossible to learn the nature of the control of accommodation, whether it involves the awareness of target nearness, the desire to keep the image clear, or a real reflex mechanism involving chromatic aberration and the Stiles-Crawford effect.

Comment: In this paper the author has attempted to investigate the mechanisms which produce accommodative responses in the eyes by means of a haploscope and two photographic systems, one designed to record changes in the radius of the anterior surface of the crystalline lens and the other to record changes in convergence.

Assuming that accommodation is a binocular function, the author arranged two targets in an optometer system in front of one eye, so that the subject, in order to see clearly, would not accommodate for one but would accommodate for 2 D. for the second and 4 D. for the third. Accommodation responses were noted in the fixing eye and convergence with both eyes by means of the photographic equipment.

From the somewhat confused results, the author believes that he has supportive

evidence of a willed voluntary control of accommodation because of a delay in reaction time somewhat greater than that ordinarily expected from a true reflex.

In the discussions of the stimulus-response mechanisms in accommodation found in the literature, there has been some uncertainty as to the precise definition of the term "reflex." As ordinarily used, it signifies a motor response which has been produced by stimuli not consciously initiated. That accommodative responses can be initiated in such a manner seems apparent when the results of clinical experiments with accommodation produced by convergence or by proximity are considered. On the other hand, the normal accommodative response to retinal image blurs presupposes some degree of visual awareness and is certainly cortical and might, for that reason, be considered to have some voluntary aspects. From the clinical standpoint there are four stimulus response systems and only four, as far as is known, which produce accommodation. There are, first the amount of accommodation produced by the normal tonus of the ciliary muscle, that resulting from the blurring of the retinal image, that due to the presence of convergence, and that dependent upon the sense of nearness. The latter, of course, can be considered as a psychic stimulus, while the retinal blur response has some elements of awareness and the other two represent purely subcortical reflex systems.

As the author indicates, considerably more work will have to be done in this field, but it would seem that more precise definitions and more attention to the known clinical aspects of the question would be helpful.

EDWIN F. TAIT

THE GLOBE

PROBLEMS OF ORBITAL IMPLANTS AFTER ENUCLEATION

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Brit. J. Ophth., 1955, *39:* 599–604

Several years ago the author described a three-quarter sphere plastic implant with tunnels through which the four recti were drawn and sutured. Later Monro-Brazil observed that if an implant had a peg buried some distance from the conjunctival wound, it would slowly perforate the conjunctiva without any visible wound being formed about it. The implant being used now consists of the three-quarter tunneled sphere combined with one or two pegs 1 mm. thick and 7 mm. long projecting from the upper part of the front surface.

The implant is inserted using the customary technique for enucleation, threading the recti muscles through the tunnels and closing the conjunctiva and Tenon's so that the pegs are buried but not included in the wound. The pegs slowly perforate the overlying tissues in two to four weeks. A semi-final acrylic implant with perforations to receive the pegs is fitted two or three months later. Frequently, as retraction occurs, the position of these openings must be changed.

Since 1951 the implant has been used in 39 patients. In two patients the implant was removed, one because of detachment of a muscle, in the other because of inflammation. A mucous membrane graft was required to close the wound in another patient. One other patient had an orbital inflammation which healed uneventfully, and in another, apparent detachment of a muscle required modification of the prosthesis because of altered position of the peg.

Disinsertion of the muscles in these patients led to a modification of the operative procedure in which the muscles remain attached to a ring of sclera. The conjunctiva is dissected almost to the equator of the globe and the cornea excised at the limbus. The contents of the eye are removed as in an evisceration. Through the corneal opening the sclera is cut so that a scleral ring containing all four muscles remains extending from the limbus to the equator. The posterior sclera is then pulled forward and the optic nerve and insertion of the oblique muscles cut. The implant, which does not have tunnels, is then introduced into the sclera ring and two small perforations made through the sclera to receive the pegs. In five cases this technique has given excellent results.

Comment: This reviewer has had no personal experience with the Arruga implant. There is some indication from the current literature that if any integrated implant will be retained, this is it. Most surgeons now recognize that the violation of surgical principles

by leaving a partially buried foreign body, is no different with acrylic or tantalum or stainless steel, than it is with any other relatively inert substance. Such procedures are doomed to failure. Arruga's implant does not seem to be such a flagrant violation of these principles, and yet it is a definite violation. The final decision cannot be made for many months or even years, but in the meantime, except in the case of the most unusual circumstances, it will be well to follow established principles and conservative techniques.

DANIEL SNYDACKER

EVISCERATION OF THE EYE WITH IMPLANTATION OF POLYVINYL SPONGE

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A. M. A. Arch. Ophth., 1955, *54:* 373–380

The solution to the problem of extrusion of implants would seem to be in finding a substance which would become totally united with and incorporated into adjacent living tissue, thus militating against any possibility of extrusion in the future. At the same time, to be entirely suitable, such an implant material would have to satisfy criteria of non-absorbability, stability, and biologic inertness. Polyvinyl-formal sponge may fulfill these criteria and the present study was undertaken to determine the reaction of the ocular tissues of the dog to the presence of this material.

The left eye of 20 dogs was either partially or completely eviscerated. Polyvinyl sponge was then inserted into these eyes and their behavior was observed over variable periods of time up to one year. In the majority of eyes the sponge was successfully retained. In such specimens the interspaces of the sponge became filled with a connective tissue that was continuous with the tissues comprising the wall of the eye. These eyes showed a remarkable tolerance toward this sponge, and in several cases the corneas became transparent over an observation period of one year. This occurred even though the endothelium was absent.

Comment: A carefully controlled experiment such as that reported here is welcomed since clinical opinion concerning orbital implants has completed a circle. Results obtained following the now common practice of inserting a Mules' sphere, although better than they used to be because of improved technique of the artificial eye makers, falls far short of prefection. The findings of these authors indicate that in instances in which evisceration is safe, satisfactory cosmetic results might be better than those now commonly obtained by the use of the technique which they describe in experimental animals. It would be most interesting to have a clinical report of results of this technique, and it is hoped that one will soon be forthcoming.

DANIEL SNYDACKER

THE LENS

AXIS TRACTION CATARACT EXTRACTION WITH VACUUM

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J. Internat. Coll. Surg., 1955, *23:* 841–846

Small changes in the technique of cataract extraction are resulting in better post operative results with fewer complications. Homatropine is instilled in the eye to be operated the night before surgery and neosynephrine (10 per cent) at one-half hour intervals the two hours preceding. Five grains of barbital are administered one-half hour before the operation.

Topical Pontocaine is instilled and a retrobulbar injection of 2 per cent procaine is made and akinesia obtained with Van Lint's injection. A superior rectus bridle suture is used.

A limbus based flap approximately 2.5 mm. wide is made and a groove made at the limbus near the base of the flap. Five corneal-scleral mattress sutures are inserted at 10, 11, 12, 1 and 2 o'clock. A keratome incision is made at 9 o'clock and enlarged with scissors. A peripheral iridectomy is made, with the assistant retracting the cornea and the surgeon drawing the iris downward toward the center of the pupil.

The author's vacuum pump is used with 42 cm., Hg vacuum. The lens is drawn forward in the visual line by means of the vacuum cup and pressure with a utility forceps at 6 o'clock. When the edge of the lens is seen it is tilted and is delivered superior pole first. The sutures are then drawn up and tied and the conjunctiva closed with a continuous suture. Pilocarpine, sulfadiazine and yellow oxide of mercury ointment are then used and the lids closed by means of a lid suture.

The eye is dressed 24 hours later and the patient allowed up. The sutures are removed the twelfth or thirteenth day after surgery and the patient discharged that day. The technique has led to better visual results, a reduction of astigmatism and fewer post operative complications.

Comment: There is no question that the judicious use of preoperative medication combined with satisfactory anesthesia and akinesia has made the operation for the removal of cataract much safer than it was a few years ago. Better instruments and sharper needles with fine sutures have prolonged the time required to operate, but have certainly reduced the instance of post-operative complications. Five pre-placed corneal scleral sutures should certainly insure adequate closure of the wound, although the presence of five double arm sutures might complicate delivery of the lens.

Removal of the lens with an erisophake is not new. Some surgeons use this method

routinely, while others reserve its use to intumescent cataracts or hypermature cataracts. The advantage of an erisophake is that it gives equal traction on the zonule throughout the entire circumstance of the lens. However, if the suction is too great, one may obtain a rupture of the posterior capsule, and if the intraocular tension is very low, it may be difficult to remove the nucleus. In the presence of fluid vitreous, a nucleus may even be lost.

The author delivers the lens head-on, although in some instances it may be easier to tumble the lens, especially if the pupil has started to contract and the lens must be moulded through a small pupillary aperture. In the tumbling procedure a lens hook placed below at six o'clock just beyond the advancing edge of the lens will frequently facilitate its delivery through the round pupil.

P. Robb McDonald

TRAUMATIC CATARACT SURGERY IN CHILDREN

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Early operation is recommended for children with traumatic cataract to prevent the development of amblyopia. The operation should be performed early while the retina still retains good function and before secondary glaucoma occurs or before atrophy begins. Frequently it is not advisable to wait until all inflammation has subsided, particularly if posterior synechise are developing.

Cataract extraction is recommended by use of the author's double section cannula in which a keratome incision is made at the limbus as distant from any corneal wound as possible. The double-barreled cannula is introduced into the anterior chamber and lavage and suction carried out simultaneously.

In patients with synechiae, membranous cataract, and lens remnants occluding the pupil a combined knife-needle hook-procedure is recommended. An inverted T-shaped incision is made in the capsule with a curved needle-knife introduced at the limbus. If the membrane cannot be cut, the limbal incision is enlarged to 3 mm. as the knife is withdrawn from the anterior chamber. A blunt hook is then introduced and the membrane caught below, withdrawn and cut.

Comment: The editor has had no experience with the author's suction apparatus for soft cataract. Although the surgical principle of removing as much of the anterior capsule as possible and then irrigating out as much of the lens substance as possible, is sound, most of the dense capsules that remain following traumatic cataracts are caused by apposition of the anterior and posterior capsule with some remaining lenticular substance. The use of a curved knife needle will undoubtedly facilitate cutting some capsules, though sharpness of the blade is more important than the curvature of the blade.

Capsulectomy with a blunt hook must always be very carefully performed. If too much traction is placed upon the capsule, irreparable damage will be done to the ciliary body causing either an intractable iridocyclitis or a retinal detachment. In many of these cases it is safer to cut the capsule with scissors in-situ rather than attempting to remove it and cut it after it has been withdrawn from the anterior chamber. The use of corticosteroids is not mentioned, but is valuable aid in the treatment of postoperative inflammatory reaction.

In treating traumatic cataracts, one must never lose sight of the fact that the penetrating injury that caused the cataract may have also damaged the posterior lens capsule and ruptured the hyaloid. In performing an extracapsular extraction in these cases, one must not be too vigorous with the irrigation in case the posterior capsule hyaloid adhesion is ruptured and free vitreous enters the anterior chamber. A most important point in the surgery is to remove as much of the anterior lens capsule as possible and remove as much of the lens substance as possible to prevent a secondary glaucoma. A large amount of lens material will gradually be absorbed and a clear pupillary opening may be obtained several months following the surgery. The injection of air into the anterior chamber following the surgery will frequently prevent anterior synechia and force any lens material out of the incision.

P. Robb McDonald

THE INTRAOCULAR PRESSURE

AN EVALUATION OF SCLERAL TONOMETRY—ITS RELIABILITY, VALIDITY AND CLINICAL APPLICABILITY

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Am. J. Optom. and Arch. Am. Acad. Optom., 1955, *32:* 391–402

All tests, psychologic, physiologic, or physical, depend for their value on reliability and validity. The term reliability refers to the repeatability of the test and indicates whether successive trials under given conditions will yield similar results. Validity expresses the accuracy with which the test meets the purpose for which it was designed, i.e., the measurement of a certain variable or function. In addition to reliability and validity, clinical tests may be judged by a third criterion, that of clinical applicability. This criterion determines whether the value of the information obtained by the test is great enough to offset such negative elements as discomfort or danger for the patient, excessive time-consumption, or the need for costly equipment and trained observers.

Scleral tonometry is not a new technique for estimating intraocular pressure, but its reliability and validity have apparently not been established. An experimental study of this procedure was therefore undertaken for the purpose of determining its reliability and validity and also of ascertaining its clinical applicability. The subjects were consecutive patients in the author's optometric practice. A Wolfe tonometer that had recently been recalibrated for use as a scleral tonometer was used in all the experiments. Scleral tonometry was performed on every patient over 30 for the first and second series, and over 40 for the third series. The data for the study include the patient's age, sex, and refractive state (equivalent sphere), as well as the tonometric measurement of intraocular tension. The average value of the tension for the sample of 80 eyes in the first experiment was approximately 22 mm. and the standard deviation was 4.5 mm. Values for myopes seem to be 2 or 3 mm. below the average. The close agreement found between the values in this experiment and those customarily found by corneal tonometry tends to establish the validity of the test. Not only are the average values similar, but the range (13 to 31 mm.) seems to be identical. However, the distribution curve for scleral tensions was skewed and this did not seem to be the case with corneal tonometry. Age, within the range of 30 to 70 years, sex, and laterality seemed to have little effect on the values.

The second experiment, which was designed as a test of reliability, was abandoned after the next 13 consecutive patients had been tested because the results obtained suggested that the first of two readings taken was the least representative. In the third experiment, therefore, three sets of readings were taken and

recorded, using the next 23 consecutive patients over the age of 40. The values obtained by discarding the first reading and averaging the other two apparently provide as reliable a measure as it is possible to get. The reliability coefficient when the first reading was discarded was about plus 0.77.

Upon completion of the experiments, the data for the 3 groups (76 patients in all) were combined to obtain a frequency distribution. The distribution curve seems to be bimodal or composed of 2 distributions which overlap in the region of 22 to 26 mm. This indicates that scleral tonometry is affected by some factor other than and in addition to the intraocular pressure. This factor may be the degree of rigidity of the sclera. If so, then between 15 and 20% of the population has scleral rigidity of such degree as to lead to unduly high scleral tonometer readings. The patients, therefore, must be divided into 3 categories: (1) those with normal pressure (readings below 25 mm. Hg); (2) those with abnormally high pressure (readings above 30 or 32 mm. Hg); and (3) those who have either high intraocular pressure or undue scleral rigidity (readings between 25 mm. Hg and 30 mm. Hg). Unfortunately, it is often in the third group with its 15 to 20 per cent of the population that a differential diagnosis is so important.

As for the clinical applicability of scleral tonometry, the author's experience with some 200 patients indicates that there are no real dangers to the patient if the instrument is used carefully. The only incidents were 2 subconjunctival hemorrhages. This complication although alarming to the patient and unpleasant for the practitioner, is not serious. Its occurrence can be tolerated if the test is valid and useful in the detection of glaucoma.

Comment: The subject of the validity of scleral tonometry which is used by optometrists as a diagnostic procedure is rather important, in view of the large number of patients whom they examine. This paper is a fair attempt at the evaluation of the instrument. The author finds that the distribution curve for scleral tensions is skewed, a fact which is not true for corneal tonometry. The bimodal distribution curve which he finds is incompatible with the nature of the intraocular pressure. He suggests that the factor which causes the lack of sensitivity of the instrument in the 25 to 30 mm. Hg range which he finds in 15 to 20 per cent of the population, is the high degree of rigidity of the sclera. This finding is not consistent with the findings of ophthalmic research and clinical experience.

Several obvious criticisms of scleral tonometry may be made. First, the presence of other tissues, namely the conjunctiva and the rectus muscles, between the tonometer footplate and the sclera, interferes with accurate measurement. With the scleral tonometer one measures not the intraocular volume displacement which the corneal tonometer determines but a variable quantity resulting from the individual variations in thickness and vascularity of the tissues overlying the sclera. For this reason the tonometer would have to be applied at exactly the same spot each time even to compare readings in the same patient. Second, without benefit of anesthesia, since the patient at least feels the applied object, there is a tendency to increase the tonicity of the orbicularis and the rectus muscles. This tends to raise the intraocular pressure. The author has overcome this objection in part by discarding the first readings for each eye.

It must be concluded that scleral tonometry cannot be regarded as comparable to corneal tonometry as a clinical tool. It should be remembered that the value of tonometry

as a diagnostic instrument is in the border-line cases, those in which moderate elevations of pressure are present, and in the subsequent follow-up of these individuals. Here a dependable instrument is quite necessary. When the tension is high or the disease advanced, digital tonometry and the other diagnostic signs such as ophthalmoscopy and visual field changes make the diagnosis of glaucoma relatively easy.

H. Saul Sugar

MANAGEMENT OF THE NARROW ANGLE GLAUCOMA

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In narrow angle glaucoma the obstruction to outflow is the result, solely, of blockage to the angle by contact between the periphery of the iris and the trabeculum. In the wide angle type, the angle is open, but the increased intraocular tension seems to be the result of an obstruction to outflow that is apparently localized within the trabeculum or within Schlemm's canal mechanism, with its outflow channels, or both.

The principal anatomic factor responsible for the narrow angle is the size of the lens, i.e., the size of the lens in relation to the anterior segment. The most important precipitating factor in narrow angle glaucoma, however, is the relative pupillary block, or functional seclusion of the pupil, or abnormal resistance to flow from the posterior to the anterior chamber.

Peripheral iridectomy is recommended as the surgical treatment of acute glaucoma when the tension is brought within normal limits by medical therapy. For cases in which the tension is insufficiently controlled by miotics, iridencleisis or iridencleisis with a hinged scleral flap is advocated. Chandler has done a modified basal iridectomy in such cases.

In the treatment of the chronic narrow angle glaucoma peripheral anterior synechiae must be prevented or disrupted by the occasional induction of intense miosis. The surgical treatment will depend to a large extent upon the age of the patient and the stage of the disease. The miotics will have an increased effectiveness after peripheral iridectomy in the borderline stages of the disease; if the disease is advanced, however, with extensive peripheral anterior synechiae a filtering operation such as iridencleisis or, preferably, anterior flap sclerotomy with basal iridencleisis is advocated.

Comment: This is a review of the clinical literature on primary glaucoma. In discussing the principal anatomic factor responsible for the narrow angle, Sternberg states that it is the size of the lens relative to the anterior segment. This is the view of Priestley Smith and cannot be considered today as the principal factor. The lens size increases with age, of course, in every eye and is an important factor in those cases where the angle itself is primarily narrow.

H. Saul Sugar

NEUROLOGY

THE COURSE OF THE FIBERS OF INTRINSIC MOTILITY (PUPILLOMOTOR FIBERS) IN THE THIRD NERVE. ANATOMOHISTOLOGIC STUDY AND PATHOGENIC CONCLUSIONS.

M. G. Lazorthes, R. Pigassou and M. J. Gaubert

Toulouse, Belgium

Bull. Soc. Belge d'Ophtal., 1955, *109:* 16–22

Isolated and unilateral mydriasis often appears as an accompaniment of cranial trauma; in patients with intracranial hematomas, its frequency varies from 30 to 50 per cent. Among the many contradictory theories advanced to explain its origin are (1) hemispheric compression; (2) sympathetic irritation; and (3) compression of the trunk of the third nerve against the base of the skull. The authors therefore investigated the localization of the pupillomotor fibers within the third nerve to see if they could clarify the situation. Their anatomic and histologic studies showed that the nerve is located about 5 mm. outside the posterior clinoid (average 4.6 mm.), and that, in the vertical plane, it lies below the clinoid (average 2.9 mm.). In addition, it comes in contact with the ridge of dura mater called the petroclinoid ligament by German authors (not the classic petroclinoid ligament). Consequently, the two points at which the nerve is vulnerable are the upper edge of the petroclinoid ligament, where it may suffer compression in the event of cranial hypertension, and the external edge of the posterior clinoid, where it may be compressed abruptly, by a lateral shift of the cerebral trunk or progressively by a hematoma of the base or a temporal involvement. Examination, confirmed by microscopic studies, shows that, after their emergence, the innermost fibers of the nerve describe a spiral half-turn. Rising in the interpeduncular space, they cross the inferior aspect and move toward the external edge; then they borrow the inferior branch of the third nerve and the nerve of the small oblique, from which they proceed to their end in the ophthalmic ganglion.

The pupillomotor fibers thus follow an exposed course and are readily subject to compression against the posterior clinoid. It is against this structure or against the posterior cerebral arteries or the posterior communicating artery that the nerve may be injured and it is at this point that the pupillomotor fibers, lying at the periphery and on the internal aspect, may be electively affected. The soundness of this hypothesis was demonstrated by the finding at autopsy of a fracture of the clinoid in a patient with unilateral mydriasis.

Comment: If this interesting theory of the course of the pupillomotor fibers is accepted, one must conclude that the dilated pupil of tentorial herniation, in brain lesions, results from traction of the medial part of the nerve against the posterior clinoid. Walsh has

reported a dilated pupil in monkeys where the superficial third nerve was damaged experimentally. The authors of this paper do not give evidence for the association of ptosis and mydriasis often seen clinically.

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PUPILLARY REFLEX SHAPES AND TOPICAL CLINICAL DIAGNOSIS

OTTO LOWENSTEIN

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Neurology, 1955, *5:* 631–644

Analysis of reflex shapes is not new. Descriptions of the patellar reflex, for example, are not limited to such details as unilateral or bilateral increase, decrease, or absence. Equally important are observations as to the shape of the reflex, whether it is spastic or clonic, inhibited or exaggerated by psychological or other factors, and whether it is limited to the proper effector muscle or muscle groups. Similarly, pupillary movements and reflexes may not only be slower or less extensive than normal, but may also show an even greater variety of pathological reflex shapes than do the deep reflexes.

The iris is an ideal indicator of autonomic reflex activity. This membrane with its freely floating edge is unimpeded by mechanical weights, and its movements, unlike those of other autonomic structures, can be recorded without even touching the body. All pupillary reactions, both of contraction and dilation, are typically integrated autonomic reflexes. Functional or organic damage to the nervous centers or pathways which normally control the iris results in characteristic changes of the reflex pattern. The fact that each of these characteristic changes is indicative of damage at a specific site within the centers and pathways of pupillary control gives them a topical diagnostic value.

The pattern of a pupillary reflex depends not only on the strength and duration of the stimulus, but also on the equilibrium of pupillo-constrictor and pupillodilator impulses present in the iris at the moment of stimulation. It is therefore necessary to standardize the experimental conditions, to eliminate as far as possible extraneous sensory and emotional stimuli, and to accurately record and analyze pupillary movements.

Pupillographic studies made under standard conditions in approximately 2,500 patients with pupillary pathology and in 300 normal subjects, as well as in many experimental animals, show that these characteristic changes occur

whenever a clinical or experimental lesion injures one of the pupillary centers or pathways.

(1) If the cervical sympathetic path is damaged, either preganglionically or postganglionically, part of the system which normally antagonizes the contraction to light is eliminated. As a result, the sympathectomized pupil is smaller than the normal one after adaptation to darkness; it contracts somewhat faster to light; and psychosensory dilation is greatly reduced in extent and speed.

(2) If a lesion is located in the diencephalon, or its connections to the midbrain fairly close to the midline the third nerve nucleus may be released from the inhibitory impulses from the cortex, thalamus, and hypothalamus which normally impinge upon it. The pupillary light reflex then assumes a square-wave shape (named the tonohaptic shape) and is less extensive than normal, not because of a lack of parasympathetic strength, but because the initial size of the pupil after adaptation to darkness is even smaller than in cases of peripheral sympathectomy; this is proven by the fact that the contraction to light is much faster than normal. Psychosensory dilation generally remains undisturbed in these cases.

(3) The pupil of the injured side in patients with non-irritative partial lesions in the third nerve nucleus or peripheral to it is normal in size or very slightly enlarged after adaptation to darkness; in diffuse room illumination, it may be much larger than the normal pupil. The reflex to light is sluggish, inextensive, and preceded by a prolonged latency period. Psychosensory dilation is undisturbed and as extensive as that of the normal dark adapted pupil.

(4) Sluggish and inextensive reaction to light is also found with a dark-adapted pupil that is smaller than normal in the presence of an irritative nuclear or prenuclear third nerve lesion. When the pupil is small and the light reflex is highly reduced or absent while the reaction to near vision is present, it is called the Argyll Robertson pupil (reflex pupillary immobility). Psychosensory dilation may be normal in cases in which the light reaction is absent.

(5) Central sympathetic irritation is accompanied by pupils that are larger than normal in both light and dark. When sympathetic irritation increases, the size of the pupil increases and the light reflex assumes a W or V shape. Pronounced irritation may result in complete inhibition and an absence of contraction to light. Psychosensory dilation is normal or exaggerated.

(6) W and V reflex shapes may also be seen in small pupils when both the sympathetic and the parasympathetic are weakened. In the case of the large pupil, there is an unstable equilibrium of two strong antagonists; in the case of small pupils, there is a similar equilibrium of two weak antagonists. The shape of the reflexes is identical, but the extent and speed of motion as well as the pupillary diameters are different. Psychosensory dilation is usually normal in cases of sympathetic and parasympathetic weakness.

All the reflex shapes described as resulting from pathological conditions at specific sites within the centers of pathways of pupillary control may also appear as transitory and reversible phenomena produced by physiologic fatigue or excitement. Fatigue is an ordered sequence of events in which the functions of

specific nervous centers are diminished and finally extinguished in a given order. By tracing the stages of fatigue through pupillographic studies, a general law of autonomic nervous fatigue may be formulated as follows: All fatigue is predominantly central in origin; cortical centers become fatigued sooner than subcortical centers, and the sympathetic sooner than the parasympathetic.

The pattern of physiologic fatigue, however, unlike those accompanying pathologic changes, which are permanent and irreversible, can be readily reversed by rest or by sympathetic stimulation provoked by sensory stimuli, emotional excitement or spontaneous thoughts. The so-called, "psycho-sensory restitution phenomenon," a phenomenon which is not limited to pupillary reflexes, but is a general principle of reintegration of fatigued or exhausted nervous centers. The absence or diminution of this phenomenon is generally associated with tonohaptic reflex shapes and, like them, is indicative of diencephalic injury.

Eight clinical cases illustrating the manner in which these principles may be applied to the syndromes most frequently encountered in clinical pupillographic work are reported in detail.

CONGENITAL HEREDITARY VERTICAL NYSTAGMUS

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J. Neurol. Neurosurg. Psychiat., 1955, *18:* 196, 198

Congenital nystagmus of the vertical type is a rare disorder of great interest to geneticists. The five cases now reported occurred in a family of pure Italian extraction and were spread over three generations. Three of the subjects were males, aged 67, 38, and 10 years; the two females were aged 15 years and 15 months, respectively. In three cases, the head movements accompanying the vertical nystagmus were rotary in type. Interestingly enough, some of these patients were unable to appreciate the nystagmus in others. An effort should always be made, therefore, to obtain histories from unaffected members of the family; otherwise, several cases may be missed. It was thought at first that the eyes of the patients with this inability must be synchronizing, but the fact that in two of them there was a considerable difference in the rate and amplitude of the nystagmus seems to make such an explanation impossible.

The movements of the head in the patients in this series diminished during fixation and increased when the subject was not concentrating. The 38-year-old man volunteered the information that he was more conscious of the head movements while concentrating and that he tried to suppress them as soon as they

appeared. Twelve members of the family have been examined and their blood groups, eye color, and other pertinent data, together with a diagrammatic pedigree, are appended to the original article. There is no known consanguinity in the matings.

The actual site of the lesion in congenital hereditary nystagmus is unknown, as none of the patients have come to post-mortem study.

Comment: Since vertical nystagmus is rare except in cerebellar lesions its occurrence in an inherited congenital form is worthy of note. The importance of obtaining an adequate family history in such patients is obvious.

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THE OPTIC NERVE SHEATH PATHWAY

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A. M. A. Arch. Ophth., 1955, *54:* 369–372

Anatomic and injection studies upon cadavers have demonstrated the continuity of the cranial subdural and subarachnoid spaces with corresponding spaces around the optic nerve. Three cases are presented in which there is evidence of transmission of particulate matter through the optic nerve sheath during life. The first patient died three months after a craniotomy for a malignant glioma of the left temporal lobe. A foreign body containing optically active foreign material was found in the left sclera. It was apparently caused by suture material introduced into the cranial cavity during the craniotomy.

In two other patients, tumor cells metastatic from the breast were found in the optic nerve sheath. In each the tumor presumably spread from the brain down the optic nerve sheath. The possibility that bilateral optic nerve sheath involvement resulted from independent blood borne metastases could not be excluded.

Comment: Although not conclusive, these observations suggest active passage of material from intracranial to optic nerve cerebrospinal fluid spaces. The converse can also occur: the spread of retinoblastoma cells backward to produce a tumor meningitis.

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THE RETINA

ELECTRICAL BRAIN POTENTIALS IN RETINITIS PIGMENTOSA AND FAMILIAL HEMERALOPIA

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Ophthalmologica, 1955, *130:* 116

Electroencephalographic studies of 25 patients with retinitis pigmentosa and 5 of their close relatives suffering from hemeralopia (impaired dark adaptation) showed a significantly increased incidence of abnormal recored (14 out of 30, or 47 per cent), as compared with an incidence of not more than 15 per cent in numerous unselected populations. Deviations from the norm were pronounced in 7 of the patients with retinitis pigmentosa and slight in the other 5. One of the two abnormal records obtained from the hemeralopic patients was markedly disturbed and contained paroxysmal features, while the other showed only a mild generalized disturbance. There were twice as many males as females in this study, but the incidence of abnormal records was about equal in both sexes. The abnormality most commonly found consisted of bilaterally symmetrical and synchronous slow waves. They usually appeared diffusely, but sometimes took the form of hypersynchronous outbursts, which became more manifest during and after hyperventilation. Electroencephalographic changes of this type are found in lesions and functional disturbances of the structures surrounding the third ventricle and of the upper brain stem. These findings seem to support the clinical impression that retinitis pigmentosa and familial hemeralopia are associated with disturbances in the hypothalamo-pituitary system.

Comment: In various studies of other authors approximately 15 per cent of electroencephalograms in persons selected at random from the population showed abnormal recordings. The demonstration by the authors of 47 per cent of pathologic EEG's in a group of 30 persons (25 cases of retinitis pigmentosa and 5 of their relatives with familial night blindness) should be considered significant in confirming the association of retinitis pigmentosa with disturbances of the diencephalic region which has long been suspected from clinical observation and animal experiments.

The abnormalities of the EEG's were of a type often found in tumors and other pathologic changes around the third ventricle and its vicinity. More frequent recordings of EEG's in patients with heredo-degenerative diseases of the fundus oculi and in atypical, poorly understood cases resembling them but of sporadic occurrence, could lead to a better understanding and classification of these diseases than we have now.

Bertha A. Klien

ANOMALIES OF THE EYE IN SO CALLED INCONTINENTIA PIGMENTI. CONTRIBUTION TO DIFFERENTIAL DIAGNOSIS AND PATHOGENESIS OF PSEUDOGLIOMA OPPOSED TO RETROLENTAL FIBROPLASIA.

H. Krümmel and L. Rausch

Ophthalmologica, 1955, *130:* 31–53

A case of so-called incontinentia pigmenti or Siemens-Bloch's pigmentary dermatosis is described in an 8-month-old girl. On the second day of her life there had appeared on the trunk and on the extremities red stippling and small vesicles the size the head of a pin, which later on changed into pustules. These temporary, but recurrent inflammatory manifestations were associated with the well-known picture of amaurotic cat's-eye. The microscopic examination of the child's eye did not reveal the suspected retinal glioma, but a congenital malformation with persistence of the hyaloid artery and of the primary vitreous body in the retrolental space, total detachment of the dysplastic retina, partial atrophy of the corneal epithelium and ciliary body and anomalies of the pigmented epithelium of the retina. The observations in this case throw a new light on previous descriptions of eye-changes associated with pigmentary dermatosis. Fourteen such cases were collected from the literature and are presented in Table 1. Uebel and his co-workers (case 13 in the table) grouped their case with those of Rieger's dysgenesis mesodermalis, and they discussed its relationship to retrolental fibroplasia, which according to Reese may be subdivided in three types, namely, retinal dysplasia, persistent hyperplastic primary vitreous body, and genuine retrolental fibroplasia. The terminal stages of these three types show considerable anatomicopathologic similarities which justify their listing under the term of rentrolental hyperplasia; but the three types may be separated primarily from the clinical point of view. In this sense the authors' case was definitely not one of retrolental fibroplasia, but cannot be definitely ranged either with the second or first type of this disease. Although the characteristic dysplasia of the retina was most severe, it was not bilateral and, except for the pigmentary dermatosis, other organic abnormalities were missing. The unilateral condition and the mild microphthalmia, the prominent connective tissue mass in the axial area behind the lens and the persistent hyaloid artery corresponded at best with Reese's second type of retrolental fibroplasia. As a result of considerations of differential diagnosis the author states that his case presents a congenital malformation, the characteristics of which are the persistence of the hyaloid artery and of the primary vitreous body with hypertrophy and metaplasia of its mesodermal portions. Detachment and malformation of the retina, dysplasia of the ciliary body and arrested growth of the bulbus are sequelae. Peculiarities were the formation of an exudate behind the retina and the start of a process of removal by migratory cells of the pigmented epithelium of the retina which had been transformed into facultative phagocytes; the hypertrophy

TABLE 1

Cases of Incontinentia Pigmenti with Ocular Anomalies Collected from the Literature

No.	Author(s)	Ophthalmologic Findings	Other Anomalies
1.	Bloch and Sulzberger	Retrobulbar glioma	
2.	Siemens	Convergent strabismus	Microcephaloid, Littel's disease, congenital cardiac defect
3.	Moncorps	Convergent strabismus, atrophy of left optic nerve, suspicion of retrobulbar glioma	Pronounced ill-tempered behavior
4.	Sulzberger and coworkers	Unilateral congenital blindness, opacity of the cornea caused by calcium, cataract, convergent strabismus, blindness of the left eye in the niece	Disturbance of development in hair, nails and teeth, dental anomalies in mother and niece. All had sparse hair on the head and defects of nails.
5.	Jäckli	Juvenile complicated cataract	Microdentism, alopecia
6.	Carol and Bour	Fundus rich in pigment despite fair-haired type; chorioidal ring	Mild rickets; no teeth at the age of nine month
7.	Heilesen	Pseudoglioma of the right eye	—
8.	Heilesen	Convergent strabismus	—
9.	Sulzberger and Bloom	Blue scleras	—
10.	Gérard	Bilateral phthisis of the eye-ball	—
11.	Haber	Blue scleras	Spasms
12.	Seidlmayer	Bilateral, temporal turning pale of papilla of optic nerve	Microcephaly, feeble-mindedness
13.	Uebel and coworkers	Ptosis, convergent strabismus; microphthalmia; spotty opacification of cornea; synechias; anomaly of structure of iris; fibroplastic tissue behind the lens	—
14.	Rein and Weidmann	Changes of fundus oculi	—

of the pigmented epithelium; and atrophy and parakeratosis of the corneal epithelium. The association of this ocular malformation with a pigmentary dermatosis suggests an oculocutaneous syndrome.

Comment: During the past three decades another oculo-cutaneous syndrome has been crystallizing out of a profusion of dermatologic and ophthalmic case reports. The skin lesion consists either of a spotty or reticular pigmentation, in many cases with a past history of a vesicular or pustuliform exanthem soon after birth.

The ocular findings, when present, are usually unilateral and suggestive of congenital anomalies or malformations. Also this author's well reported case was one of arrest of embryonic growth with slight microphthalmia and persistence of the primary vitreous. The illustrations also suggest failure of primary coaptation of the retina and of the formation of secondary vitreous.

Inflammatory lesions could, but need not be assumed to explain the firm attachment between primary vitreous and retina in such cases. Thus, the eye findings in this and similar cases have not been contributary in the decision between the two main hypotheses advanced by the dermatologist concerning the pathogenesis of this syndrome, namely an inflammatory versus a congenital, or even a genetically predetermined origin.

In the cytologic descriptions the author over-emphasizes the activities of the pigment epithelium, such as simple proliferation and production of phagocytes, which are found in a great variety of other pathologic conditions and should not be linked up with the "incontinentia pigmenti" described by the dermatologists.

The pigment of the skin lesion lies in the stratum corium of the cutis with nonpigmented basal cells overlying it. One hypothesis assumes a pathologic alteration, possibly congenital, of the melanoblasts (basal cells), which permits an immediate, rapid, and complete migration of the just formed pigment into the underlying cutis, instead of being cast off eventually with the stratum corneum.

The ophthalmologist's contribution to a better definition of this syndrome should be a careful investigation of the early history of the patient and of the condition of the skin in all cases of sporadic, unilateral ocular anomalies, malformations and atypical lesions of the fundus.

BERTHA A. KLIEN

STUDIES ON DEVELOPING RETINAL VESSELS. I. INFLUENCE OF RETINAL DETACHMENT

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Brit. J. Ophth., 1955, *39:* 449–456

The choroidal circulation, which is apparently responsible for maintaining retinal nutrition in the early stages of the normal development of the human retina, gradually becomes inadequate as the metabolic needs of the growing retina increase. As a result, new vessels bud into the retina from the hyaloid artery at the disk. The choriocapillaris, however, continues throughout life to supply the outer retina to a depth of about 130 microns and in health this zone is never invaded by retinal capillaries. The sharp demarcation of the avascular area in the outer retina suggests that the choriocapillaris is capable of supplying nutrition into the retina for only a limited distance and brings up the question of the effect that would be produced on the growth of retinal vessels by separation of the retina from the choroid.

Inasmuch as the normal pattern of vascular growth in the developing kitten retina is in every way comparable to that in the human retina, retinal detachment was induced in a series of adult cats and kittens from 3 to 5 days old.

Evaluation of the results after periods varying from 8 to 36 days showed that, although retinal detachment has no apparent influence on the growth of retinal vessels in the adult cat, it has a profound effect on the developing retinal vessels of the kitten. After artificial detachment of the retina, the vascular changes so caused take over 8 days to develop and are well established after 18 days. They are twofold: (1) an outward proliferation of vessels to form a plexus on the outer retinal surface, and (2) an inward proliferation of vessels to form glomerular tufts in the vitreous. These findings are in accord with the hypothesis that a vasoformative stimulus is elaborated in the retina in low oxygen tensions, such as would result from choroidoretinal separation, and, conversely, that such a stimulus is normally opposed or destroyed by higher oxygen tensions. Indeed, the effects of retinal detachment are very closely analogous to those following oxygen vaso-obliteration. In the latter case, the inner layers of the retina are rendered hypoxic by closure of the retinal vessels while the outer layers continue to be adequately served by the choroidal vessels, whereas in the former case the outer layers are rendered hypoxic through detachment while the inner layers continue to be supplied by the retinal vessels. It is to be remembered, however, that in the developing retina the oxygen supply to the inner layer is presumably less than the demand since the vessels are growing into it.

The full significance of these findings cannot yet be assessed, but the similarity between the intravitreal proliferations obtained by retinal detachment and those seen in Stage I retrolental fibroplasia is worthy of note. The possibility that some degree of retinal detachment may play a part in cases of retrolental fibroplasia in which supplemental oxygen has not been given should be seriously considered in future studies of this disease.

STUDIES ON DEVELOPING RETINAL VESSELS. II. INFLUENCE OF RETINAL DETACHMENT ON OXYGEN VASO-OBLITERATION

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Brit. J. Ophth., 1955, *39:* 457–462

Experiments have shown that retinal detachment prevents the obliterative effect of oxygen on the ingrowing vessels of the kitten retina. Close apposition between the retina and the choroid seems, therefore, to be necessary for the operation of the vaso-obliterative phenomenon. Since this phenomenon also depends on the concentration of oxygen, the logical conclusion is that once the retina is detached, effective levels of oxygen no longer reach the retinal tissue. The maximum experimental period, however, during which the vessels of the detached retina were observed in hyperoxia was 12½ hours, and this naturally

led to the question whether a longer period of exposure might not permit the oxygen to diffuse across the subretinal space and reach the retina in sufficient concentration. Accordingly, a fresh series of experiments was undertaken to determine the effect of prolonged oxygen exposure on vaso-obliteration in the detached kitten retina. The first experiment confirmed the previous observations that retinal detachment prevents the vaso-obliterative action of oxygen, and showed that this is so even when a degree of ambient hyperoxia that normally leads to total vaso-obliteration is maintained continuously for four days. There is a striking difference between the attached and detached halves of the retina in a kitten exposed to 70–80% oxygen for four days. It seems that effective concentrations of oxygen are unable to reach the detached retina either because diffusion is inadequate or transfer is impaired. The possibility that there are differences in reactivity to oxygen between the attached and detached retina cannot, of course, be excluded, but is unlikely.

The findings in the second experiment, in which the growth of vessels extending through the detached retina to form a network on its undersurface are not easy to interpret, because, although the behavior of the detached retina was entirely different from that of the attached retina, neither the extent nor the site of detachment during the actual period of oxygen exposure was known and because abnormal vasoproliferation has been shown to follow detachment alone, without oxygen exposure. Consequently, the extent to which the varying degrees of vasoproliferation obtained were due to oxygen vaso-obliteration, to the modification of vaso-obliteration by detachment, or to detachment alone, cannot be determined.

Comment: In the first series of experiments the authors show conclusively that hypoxia produced in the immature retina by separation from the choroid leads to an increase of the vasoformative stimulus within the retina. The result is a profuse growth of new vessels, mainly toward the outer surface of the retina, but occasionally also toward the vitreous.

This similarity between the end results from hypoxia due to detachment of the underdeveloped retina and hypoxia from oxygen obliteration should be kept in mind when confronted with a premature which shows the first stage of retrolental fibroplasia without having received supplemental oxygen. A careful search for low retinal detachments in such cases may lead to a better understanding of the "irreducible minimum" of Retrolental fibroplasia which some predict, and thus may reduce the danger of laxity in oxygen control.

Of special interest in the first series of experiments was the interval of eight days before the vasoformative stimulus manifested itself. It raises the question whether in older kittens (the oldest used in the first series was 5 days) this interval might not be shorter thus throwing light upon the somewhat confusing fact that the manifestations of Retrolental fibroplasia take longer to appear in the smaller prematures.

It seems certain that the degree of immaturity of the retina is a deciding and modifying factor in the production of the vasoformative stimulus. Detachment of the retina in adult cats had no vasoformative effect upon the retinal vessels.

The second series of experiments did not result in clear cut information of immediate clinical applicability but are of an interesting variety just the same.

It is valuable knowledge that a detachment of the immature retina prevents the vasoobliterative action of high concentrations of oxygen and the inward growth of new vessels so characteristic of this condition; but that after an interval the detachment itself produces an outward and sometimes a combined out and inward growth of new vessel. Thus, no absolutely characteristic histologic, and, even less so, clinical picture arises from these two types of hypoxia.

BERTHA A. KLIEN

STATISTICS ON 100 CASES OF RETINAL DETACHMENT SURGERY

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J. Iowa State Med. Soc., 1955, *45:* 473–476

A single operative technique was used upon 100 consecutive patients with retinal detachment. The conjunctiva is opened and one or more extraocular muscles are resected from the globe. A 1.5 mm. Walker or Pischel pin is inserted into the sclera with the coagulation current from a Thermophore instrument. The pin is placed as close as possible to the hole or tear in the retina and the pin located with the hand ophthalmoscope. A pin is then inserted through the sclera to enter the subretinal space posterior to the hole. Other pins are placed just above and immediately below the tear. After the hole has been outlined in the sclera with the pins, a 0.5 mm. Kronfeld tip is used to make a light barrage from the superior ora serrata around posterior to the hole and back to the ora serrata inferior to the hole. A cutting current is used to place a double row U-shaped barrage around the hole. The pins are then removed and the subretinal fluid usually drains through the holes made by the pins. If ophthalmoscopic examination indicates the retina to be elevated, an opening is made into the sclera and the subretinal fluid removed using an eye dropper as suction. The patient is kept flat in bed for seven days, and the dressings are changed every other day. He is allowed up on the seventh postoperative day and is discharged from the hospital on the tenth postoperative day.

The results were tabulated on the basis of improvement of vision and reattachment of the retina. In the entire series there were 68 successful operations and 32 failures. In eyes with the lens present, there were 54 successful operations and 21 failures. In 25 cases of aphakia, there were 14 successful operations. The average age of the patients was 54 years, but 72 of the 100 were over 50 years of age. Eighty-four per cent of the eyes with re-attachment obtained 6/15 vision or better.

It is concluded that nearly every detachment of the retina should be treated surgically. Accurate diagnosis must exclude intraocular neoplasm, proliferative diabetic retinopathy, Coats' disease, Harado's disease and toxemia of pregnancy. Patients whose difficulty is due to these conditions should not be operated upon but, if there is any doubt about the diagnosis, the patient should be treated as an idiopathic detachment of the retina.

Comment: The authors' statistical analysis of the surgical results in 100 consecutive, unselected cases of retinal detachment resulted in some surprising revelations, for instance that the time which had elapsed between surgery and the noted onset of the detachment was not as deciding a factor in functional as well as anatomic good surgical result as one might think, or that the age of the patient as such is not too important in the final outcome of the operation.

The overall result of 70 per cent successful surgery (cases with only anatomic cures without improvement of vision were listed as failures) points to an exquisitely detailed pre-operative evaluation of each case and one wishes that the second part of this study, the type of the detachment and the differential diagnosis, which the authors announce, would appear soon. It also seems that the operative technique used was one of the least traumatizing, since in a few cases up to five and six operations were performed with final good visual results.

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SYSTEMIC DISEASE

RESULTS OF SPLANCHNICECTOMY ON PATIENTS WITH HEMORRHAGIC HYPERTENSIVE RETINITIS

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New England J. Med., 1955, *253:* 398–403

The term "hemorrhagic hypertensive retinitis" was chosen because of its simplicity and because, to the average clinician, as well as in actual fact, the development of hemorrhagic fundi is the best indication that hypertension is entering a serious phase, often referred to as malignant. Classification into the 4 grades of Keith, Wagener, and Barker or the 4 types of Smithwick and Palmer and Muench provides no hard-and-fast rules for the selection of patients according to the therapy to be used. Prognosis after splanchnicectomy or drug treatment, for example, depends more on kidney function than on the mere existence or absence of papilledema. The patients with hemorrhagic fundi (grades 3 and 4 hypertension), however, are the ones who most need life-saving treatment because of their grave prognosis. Although the indications for splanchnicectomy have been reduced by the advent of new and more effective hypotensive drugs, the procedure is still valuable and should be done to prolong life in patients whose prognosis is poor but whose kidney and cardiac function is still adequate enough to justify surgical intervention. Sympathectomy may also prove to be the treatment of choice for certain young patients, because by it they may be freed from lifelong dependence on drugs. The survival rate up to 10½ years in 206 patients with hemorrhagic fundi who were subjected to sympathectomy and splanchnicectomy during the period from 1935 through 1949 was determined and compared with the expected survival rate for medically treated patients before the advent of the new hypotensive drugs. Cumulative figures formed the basis for the survival rate in the patients with grade 3 hypertension because this was the statistical method used by Keith, Wagener, and Barker in their control series and because these patients corresponded most closely in selection with theirs. The rate so calculated was 46 per cent in 10½ years as compared with an expected survival rate of 0 per cent according to Keith, Wagener, and Barker. The rates in the grade 4 patients are the relative survival rate figures compared with expected survival—the so-called 1x ratio—used by Palmer and Muench. The relative survival rate in these grade 4 patients, who corresponded to those of Palmer and Muench, was 39.9 per cent in 6½ years, as compared with an expected rate of 5.6 per cent. At 10½ years the survival rate was 33.4 per cent.

The operative mortality in the patients with grade 3 disease was 2 per cent;

in those with grade 4 disease it was 6 per cent. Blood pressure was reduced to a satisfactory level in 67 per cent of the survivors with grade 3 and 81 per cent of those with grade 4 disease. Cardiac status in patients with enlarged hearts or abnormal electrocardiograms was improved in about half the patients in the grade 3 group and in about one third of those in the grade 4 group. Hemorrhages in the fundi disappeared in 84 per cent of the patients with grade 3 disease and papilledema and hemorrhages disappeared in 100 per cent of those who had grade 4 disease. Many of the patients in both groups are apparently "cured" of the disease; and many others feel well (74 per cent of the survivors in the grade 3 group; and 75 per cent of those in the grade 4 group). In addition, many who may eventually succumb to the disease are enjoying a few extra years of life in relatively good health.

Ability of the kidneys to concentrate urine to a specific gravity of at least 1.020 is apparently the best prognostic test for a good result in these two groups.

DRUG THERAPY IN HYPERTENSION WITH HEMORRHAGIC HYPERTENSIVE RETINITIS

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New England J. Med., 1955, *253:* 395–398

Treatment with the newer hypotensive drugs appears to offer more to patients with severe hypertension and hemorrhagic eye grounds than any previous medical therapy. The effects of therapy on the final outcome of hypertension cannot easily be evaluated, because the condition may be benign, with no influence on longevity, or rapidly progressing and fatal. The prognosis in untreated patients with hemorrhagic eye grounds, however, has been shown to be invariably poor and for this reason patients with grades 3 and 4 hypertension, as classified by Keith, Wagener and Barker, were chosen for this study. In order to eliminate patients whose disease was in the terminal stages, none who had been under treatment for less than 4 months were included in this series. Curable causes of hypertension were ruled out by careful investigation before therapy was begun, and in addition all the patients had the following studies: 7-foot chest roentgenogram for heart size, electrocardiogram, cold-pressor test, determination of phenolsulfonphthalein excretion, urea clearance and nonprotein nitrogen concentration test, urinalysis and complete blood counts. An intravenous pyelogram was obtained in most cases. Some 79 of the better risk patients were removed from this series when they were selected for splanchnicectomy. Patients who were to be treated with the potent drugs were first placed on *Rauwolfia serpentina* (Raudixin), 50 to 100 mg. three times daily, or reserpine

(Serpasil), 0.1 to 0.25 mg. three times daily, for from 3 to 6 weeks at home. The patients were then hospitalized and one of the autonomic blocking agents was usually added. Hexamethonium was used at first but has been virtually abandoned in favor of pentolinium (Ansolysen), with its apparently more prolonged and predictable effect. Although none of the patients showed adequate response of blood pressure to the "priming" treatment with *R. serpentina*, it did permit the use of smaller doses of the blocking agents with fewer side actions and smoother blood pressure curves. Adjustment of the dose was sometimes troublesome but could usually be accomplished satisfactorily. The overall goal was to keep the patients living at a diastolic pressure between 90 and 110 mm. Hg in the standing position. With diastolic pressures at these figures, regardless of systolic pressures, the degenerative signs of renocardiovascular disease usually subsided and symptoms were controlled. While in the hospital, the patients were taught to take and record their own blood pressures to guard against possible dangers from the drugs. The patients must be followed closely for several weeks after discharge but once the dosage has been stabilized, the intervals between visits can be extended considerably. The period of treatment has ranged from 4 to 31 months, and analysis of the results obtained in the group with grade 3 hypertension shows that 42 of the original 56 patients are still alive; 53 had a significant drop in blood pressure and 34 showed improvement in the fundi, with absorption of hemorrhages and exudates. In the group with grade 4 hypertension, 13 of the original 22 patients are still living; and 16 showed a significant drop in blood pressure. Evidence of severe renal impairment was found in 17 patients in this series before treatment was instituted, and uremia proved to be the principal cause of death; cerebrovascular accidents were a close second and myocardial infarction, congestive heart failure and hypertensive encephalopathy accounted for the remainder.

Comment: These two publications from the Lahey Clinic are representative of the improved prognosis for patients, with severe hypertension and hemorrhagic retinopathy, resulting from newer methods of therapy.

The first paper reports the dramatic change in survival rate resulting from splanchnicectomy in these severe hypertensive states. Five-year mortalities have been reduced from 70 to 80 per cent down to 20 to 30 per cent in the Grade 3 retinopathies and from 90 to 95 per cent down to 50 to 60 per cent in the Grade 4 group. This is accomplished with only a 3 per cent operative mortality. Furthermore, 90 per cent of all survivors had complete clearing of hemorrhages and exudates.

The results reported in the second paper with the use of newer hypertensive agents (the central acting rauwolfian derivatives and the ganglionic blocking agents, such as pentolinium) are equally impressive, but the follow-up periods are much shorter. In agreement with many other clinics, dramatic improvements are reported not only in survival rate, but in the absorption of retinal hemorrhages and exudates. It behooves ophthalmologists to acquaint themselves with agents available, their sites of action, and the vastly improved outlook for the patient with advanced hypertensive retinopathy.

BERNARD BECKER

THERAPEUTICS

THE PENETRATION OF AUREOMYCIN, TERRAMYCIN AND CHLORAMPHENICOL IN THE OCULAR TISSUES

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Ophthalmologica, 1955, *130:* 1–8

In superficial inflammation of the eye the therapeutic value of locally applied Terramycin, Aureomycin and chloramphenicol is well established. Each of them shows a suitable penetration into the cornea and the superficial tissues. The choice among these three may depend largely on the sensitivity of the infecting agent, which can be tested *in vitro*.

When, on the other hand, infections of the inner eye are concerned, the major problem will be to obtain a therapeutic effective concentration of the antibiotic on the spot. None of the three antibiotics is suitable for subconjunctival injections. We have to depend therefore on the penetration through the blood-aqueous barrier only. It is in this respect that the difference among these three antibiotics is most spectacular.

The penetration of chloramphenicol after oral administration is far superior to the penetration of Terramycin and Aureomycin under similar circumstances.

Regardless of the outcome of the sensitivity tests, if there were any, chloramphenicol should be given priority in cases of intra-ocular infections. Should this antibiotic fail, a combination of penicillin 4 million units intramuscularly daily and streptomycin 200 mg. subconjunctival every other day should be preferred to the use of Terramycin and Aureomycin *per os*.

Chemical substances can pass the blood-aqueous barrier in two ways (Brit. J. Ophth., 1951, *35:* 614; J. Physiol., 1948, *107:* 141, and 1950, *110:* 416). If they are fat soluble, they pass directly through the cell membranes, the rate of entry being proportional to the lipoid solubility, whereas the molecular size is of secondary importance. Fat insoluble substances, to which belong all the charged ions, cannot take the route through the cell membranes, but have to enter through intercellular spaces. The rate of entry is inversely proportional to the size of the molecules, the limit of which seems to be a molecular weight of about 500.

From this it will be clear that the permeability of the barrier to pharmaceutical compounds decreases as the lipoid solubility is lower, the ionization is more complete, and the molecular weight is more substantial.

Streptomycin (sulphate or hydrochloride), Terramycin (hydrochloride), Aureomycin (hydrochloride) as well as penicillin sodium are dissociated into charged ions when dissolved, and have a low lipoid solubility. In addition, the

molecular weights are of the order of 740, 450, 440 and 330 respectively, which characterizes these substances as poor penetrators, as they must enter the eye through the cellular spaces. Chloramphenicol with a fat solubility 10,000 times greater than penicillin readily passes the barrier through the cell membranes despite its molecular weight of 335.

Comment: This study confirms the earlier impressions of Leopold et al. and Langham of the superior intra-ocular penetration of systemically administered chloramphenicol as compared to other antibiotics. The authors support the use of chloramphenicol for intra-ocular infections and of each of the agents studied for external infections.

IRVING H. LEOPOLD

TREATMENT OF SUPERFICIAL OCULAR INFECTION WITH A POLYMYXIN-BACITRACIN OINTMENT (POLYFAX)

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Brit. J. Ophth., 1955, *39:* 557–562

The perfect antibiotic preparation for use in ocular infections would be one that was lethal to all ocular pathogens but non-irritating when applied to the eye; one to which sensitive organisms would not be able to develop resistance; and one that would not give rise to allergic reactions. As yet, it is not possible to fulfill all these conditions, but the antibiotics bacitracin and polymyxin satisfy most of them when used together. Bacitracin is effective against gram-positive organisms and the gram-negative cocci and has therefore a range very much like that of penicillin. Polymyxin is active against the gram-negative bacilli, including the *Pseudomonas pyocyaneus*. As there is no antagonistic action between the two antibiotics, they together cover the whole range of pyogenic organisms commonly causing eye infection.

Both bacitracin and polymyxin are suitable for topical application but have disadvantages when given systemically. Bacitracin is highly nephrotoxic and save in exceptional circumstances is unsuitable for systemic therapy. Polymyxin is less toxic, but it may produce neurotoxic side effects. As there is now such a wide choice of antibiotics, it is good practice to use those which are toxic when given systemically for topical application whenever possible, reserving those more suitable for systemic use for this form of therapy. Susceptible organisms rarely develop resistance to polymyxin either *in vivo* or *in vitro*. Bacterial resistance to bacitracin can be developed only with difficulty.

An ointment consisting of 400 units of bacitracin and 10,000 units of polymyxin "B" per gram of petrolatum was tested for efficacy both experimentally

and clinically in a variety of ophthalmologic infections. Stability was ensured by the petrolatum, which provided an anhydrous base. Application of the ointment to the lids four times a day for the first week and then twice daily for another two or three weeks led to the complete disappearance of all signs and symptoms in 24 of 33 patients with ulcerative blepharitis. In six others, recurrence followed the cessation of treatment, but reapplications have kept the condition under control. Three patients were not benefited, although one showed temporary improvement. Healing was obtained rapidly in each of 20 cases of nonspecific corneal ulceration treated with the bacitracin-polymyxin ointment. Applications were made twice a day and in addition atropine drops were instilled daily in all but two cases. Excellent results also followed the prophylactic use of the ointment in 123 cases of corneal injury, 88 of which were due to embedded foreign bodies and 35 to abrasions. Healing was uneventful in 115; in 8, moderate corneal infiltration occurred but settled within a few days, and only 5 required carbolization. No allergic responses occurred in any of these 176 patients. Topical application of bacitracin-polymyxin ointment may therefore be considered a practical and effective method of treatment.

Comment: The mixture of polymixin and bacitracin produces an antibiotic combination that has a broad antibiotic spectrum *in vitro* and possibly *in vivo*. The present studies indicate that this combination can be used for a variety of external infections and as a prophylactic agent.

IRVING H. LEOPOLD

TREATMENT OF VERNAL CONJUNCTIVITIS

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Brit. J. Ophth., 1955, *39:* 540–544

The etiology of vernal conjunctivitis has not been established, although it is supposed to have an association with allergy. No specific therapy is available, but palliative measures may be used until the disease subsides. The effects of various forms of therapy have been evaluated by the author on the basis of his experience with 1050 cases, 350 each of the irritative, limbal, and palpebral types, seen in the course of several years. The investigations in each case included the complete blood picture; repeated stool examinations for worm infestation; conjunctival scrapings stained with Leishman's stain for eosinophils (blood eosinophils up to 3 per cent and conjunctival eosinophils up to 3 per field were taken as normal), and ear, nose, throat, and skin examinations for evidence of allergy.

A change from a hot to a cold climate was found to be by far the best palliative. Heat and a dusty, dry atmosphere aggravate the condition, which is not so common in the humid climate of East Pakistan as in the dry, hot climate of West Pakistan. Diet, which has so far received little attention, was claimed by the patients to be a factor in the recrudescence of symptoms in 14 per cent of the cases. Whether the aggravation results from exogenous or endogenous sensitization or by a mere reflex action, is not known. Onions may be taken to irritate the eyes by their volatile vapors, and spices and other foods by reflex action. Treatment of associated intestinal parasitosis and of allergic conditions of the skin and the ear, nose, and throat had a remarkably beneficial effect on the vernal conjunctivitis, the degree of relief and control of relapse rate secured being approximately equal to that obtained by cortisone therapy. Cortisone, used topically, is the drug of choice, but it must be used for the whole season to be of real value. It was the only drug that proved effective in the palpebral type of vernal conjunctivitis, which is the most resistant. X-ray treatment was tried in a few cases, but the results were not at all encouraging.

Comment: Alimuddin has seen more cases of vernal conjunctivitis than any one else in the world. While he adds little new in this review he does demonstrate with a carefully controlled series that change of climate and cortisone are the best treatment. Treatment by means of x-rays should continue to be discouraged.

ALSON E. BRALEY

"NAPHAZOLINE," AN EFFECTIVE CURATIVE IN THE TREATMENT OF IRIDO-CYCLITIS AND GLAUCOMA

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IN COLLABORATION WITH F. A. NELEMANS

Utrecht, The Netherlands

Ophthalmologica, 1955, *130:* 85–93

"Naphazoline", here used to designate a watery naphazoline-nitrate solution has a decongestive effect when applied locally to the mucous membranes. It also proved curative when tested clinically in a patient with acute bilateral iridocyclitis. Intraocularly, naphazoline causes a moderate dilatation of the pupil, but this action alone did not seem to offer an adequate explanation of its beneficial effect in iridocyclitis. Living animals were therefore used in investigating its intraocular properties. Tests showed that fluorescein injected into an auricular vein of a rabbit appeared later and more slowly in an eye treated with naphazoline than in one that was untreated. The exchange of substances in the

blood with the intraocular fluid in the anterior chamber of the eye was thus shown to be influenced by the instillation of naphazoline into the conjunctival sac. On the assumption that naphazoline would reduce the intraocular pressure by reducing the production of intraocular fluid, it was used in a patient with unilateral glaucoma, in whom a cataracta brunescens on the right lens had been diagnosed 16 years earlier. The lens was greatly enlarged and was considered to be the principal cause of the glaucoma, the most striking symptoms of which were edema of the corneal epithelium, congested episcleral veins, a moderately dilated pupil, and pain. After instillation with 1/1000 naphazoline for 15 minutes, the corneal edema disappeared; the diameter of the pupil increased from 4 to 6½ mm.; and the intraocular pressure was reduced. After the pressure had been lowered by naphazoline but had not yet been normalized, two drops of DFP (0.05 per cent diisopropylfluorophosphonate of the firm of Labaz) were administered and promptly led to a marked reduction of pressure and narrowing of the pupil. The patient continued to take naphazoline 3 times daily, but as the pressure had reached 10/7.5 Schitz, its administration was stopped and after the second day no therapy was applied. After that, the intraocular pressure was normalized to 6/7.5 Schitz. Naphazoline therefore seems to be an important therapeutic asset in the treatment of some forms of glaucoma.

Comment: Naphazoline (or 2 (l-naphthylmethyl) imidazoline or "Privine") is recommended as adjunct local therapy in iridocyclitis and primary glaucoma. The author feels that this sympathomimetic agent reduces formation of intraocular fluid, cuts down on the permeability of the blood aqueous barrier and reduces inflammatory signs. No chemical or experimental comparative tests were made with other well known sympathomimetic agents to demonstrate any superiority of this particular compound for local ocular use.

IRVING H. LEOPOLD

HYALURONIDASE IN THE TREATMENT OF EXOPHTHALMIC OPHTHALMOPLEGIA

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Lancet, 1955, Sept. 10, pp. 537–538

An intense and often rapidly developing edema of structures within the orbit explains the protrusion of the globe and the oculomotor paresis in exophthalmic ophthalmoplegia. The edema involves the eyelids and the conjunctiva, throwing the latter into red, turgid folds in the acute phase. The threat to the cornea is sometimes met by tarsorrhaphy, and in the worst cases Naffziger's transfrontal orbital decompression is resorted to. Irradiation of the pituitary gland

has been done to inhibit the output of the thyrotropic hormone thought to be the primary cause of the orbital changes. The results have been disappointing and radiotherapy has more recently been applied to the orbit itself with some encouraging results. Cortisone and corticotrophin cause an improvement in the conjunctival edema and chemosis but very little change in the exophthalmos and ophthalmoplegia.

The patient, aged 53 years, presented himself with classical symptoms of thyrotoxicosis. He was treated with methyl thiouracil and thyroid extract with much improvement in his general disease. The exophthalmos, however, increased; there was marked edema of the conjunctiva, and an ophthalmoplegia developed. Radiotherapy to the orbit was without value. One thousand units of hyaluronidase dissolved in 0.4 cc. of 1 per cent procaine was injected directly into the conjunctiva of the worst eye, the other serving as a control. Within 24 hours of the injection there was a distinct decrease of the edema with improvement with each subsequent injection. Injection into the orbit was apparently without value.

Comment: It is always risky to evaluate the merits of a given therapy on the basis of its effect in one case. In this particular report, however, the authors have seemed to demonstrate, and their pictures support their statements, a definite effect of injections of a preparation of hyaluronidase on the edema of the conjunctiva and surface of the globe in a severe case of exophthalmic ophthalmoplegia. They wisely allowed one eye to remain untreated while they carried out their initial injections on the other eye. Although the authors were satisfied as to the effectiveness of repeated injections beneath the conjunctiva upon the edema of tissues, they could not duplicate their results as far as improvement in the ophthalmoplegia was concerned by injections deeper in the orbit. The reader who might be prone to try such injections in similar situations must be cautioned to keep the volume of any given injection small, as did the authors, so as not to further embarass the metabolic interchange at the limbus of the eye by increasing the passive congestion that is already present in the collarette of boggy conjunctiva surrounding the cornea.

JOHN W. HENDERSON

PERMANENT BILATERAL BLINDNESS FOLLOWING THE USE OF HEXAMETHONIUM CHLORIDE

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A. M. A. Arch. Ophthalmology, 1955, *54:* 422–424

Hexamethonium is a quaternary ammonium compound widely used to lower high blood pressure and to reduce bleeding in extensive surgical operations. Its effect on the eyes, of course, include mydriasis and cycloplegia. In addition to the many systemic complications that may accompany its use, various

authors have reported other ocular manifestations, such as a fall in intraocular tension, clearing of exudate and hemorrhage in the retina, hemianopsia, temporary unilateral blindness, epiphora, periorbital edema, and acute glaucoma. The need for caution in the use of antihypertensive agents such as the quaternary ammonium compounds is illustrated by the case of a 34-year-old woman who was admitted to the hospital complaining of breathlessness on exertion, blurred vision, and a vague pain in the left flank, all of 2-weeks' duration. She had known of "high blood pressure" for about a year. Hexamethonium therapy was decided on and she was given 6 mg. of hexamethonium chloride intramuscularly. The blood pressure was recorded as 240/136 and was taken at 1-minute intervals thereafter. At the fifth blood pressure reading (180/110) she complained that her vision was blurred. Because the cycloplegic action of hexamethonium was known to the physician in charge, no concern was felt and no ocular examination was made. A few minutes later, however, she became totally and permanently blind. The retinal signs and symptoms found in this patient were almost identical with those caused by systemic collapse or exsanguination or both. The precise method by which the effect is produced is not known, but among the mechanisms that may be suggested as the immediate cause are hemoclastic shock, anaphylactic crisis, and toxemia due to hemolysis.

Comment: The sudden loss of vision in this patient indicates the caution and study required with antihypertensive agents until one is certain of their ocular effects. In addition to the known effects on the pupil and the ciliary muscle, particular attention must be directed toward the intraocular pressure. The ophthalmologist must pay particular attention to any visual complaints occurring during administration of these drugs.

The article "Drug Therapy in Hypertensive Retinitis" condensed elsewhere in this issue indicates how valuable hexamethonium chloride and related compounds are in the treatment of hypertension. Despite their wide use, they have many unpleasant side effects and the decision to use one of them must never be undertaken lightly.

Of the agents which produce ganglionic blockade more or less exclusively, tetraethyl ammonium chloride was the first to be discovered. It was soon learned that this compound was effective only when injected intravenously and also only for a short period of time. In due time came hexamethonium which proved to be fairly effective on oral administration and to have a duration of action of several hours. This made it feasible for clinical trial. It was soon clear, however, that the ganglionic blocking agents act indiscriminately upon the ganglia of both the parasympathetic and the sympathetic systems and that you cannot produce inhibition of the former without a corresponding degree of inhibition of the latter. This is the pharmacological background for the actions of hexamethonium which W. D. M. Paton has portrayed so graphically in his description of the hexamethonium man. (Cited by Dragstedt, C. A., Arizona Medicine, 1955, *12:* 409–413.)

"He is a pink complexioned person, except when he has stood for a time, when he may get pale and faint. His handshake is warm and dry. He is a placid and relaxed companion; for instance, he may laugh, but he can't cry because the tears cannot come. Your rudest story will not make him blush, and the most unpleasant circumstances will fail to make him turn pale. His collars and socks stay very clean and sweet. He wears corsets and may, if you meet him out, be rather fidgety (corsets to compress his splanchnic vascular pool, fidgety to keep the venous return going from his legs). He dislikes speaking much unless helped with something to moisten his dry mouth and throat. He is long-sighted and

easily blinded by bright light. The redness of his eyeballs may suggest irregular habits and in fact his head is rather weak. But he always behaves like a gentleman and never belches or hiccups. He tends to get cold and keeps well wrapped up. But his health is good; he does not have chilblains and those diseases of modern civilization, hypertension and peptic ulcer, pass him by. He is thin because his appetite is modest; he never feels hunger pains and his stomach never rumbles. He gets rather constipated so that his intake of liquid paraffin is high. As old age comes on he will suffer from retention of urine and impotence, but frequency, precipitancy and strangury will not worry him. One is uncertain how he will end, but perhaps if he is careful, by eating less and less and getting colder and colder, he will sink into a symptomless, hypoglycaemic coma and die, as was proposed for the universe, a sort of entropy death."

USE OF SULFIRGAMIDE IN EXTERNAL DISEASES OF THE EYE

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Am. J. Ophth., 1955, *40:* 406–411

Trial in over 300 patients indicates that sulfirgamide is of definite value in the topical treatment of infections of the outer eye. Its major indications are acute bacterial conjunctivitis, inclusion conjunctivitis, and chronic infections of the eyelids, such as blepharitis, meibomitis, and conjunctivitis, especially of staphylococcal origin.

In general, like other sulfonamides, its results in acute infections were very good. In some instances, the response was not as striking as that noted from the use of antibiotics, when these are effectual. On the other hand, instances of superiority to previously tried antibiotics were also encountered. In chronic infections its effectiveness and limitations were found to be about the same as the antibiotics now available, and its use offers another valuable means of treatment.

Unfortunately, like every other medicament so far available for ophthalmic use, except possibly iodine, sulfirgamide is of no value in the treatment of infections due to other types of viruses. Like other sulfonamides, it is not recommended for central corneal ulcers, especially those due to *Pseudomonas aeruginosa*, where specific antiobiotics are the drugs of choice.

The relatively low incidence of allergy and irritation as compared to other sulfonamides and antibiotics is a point in favor of its use in all infections for which it is indicated. In prophylactic treatment of ocular injuries, it appears to be valuable as well as safe, and clinically does not seem to delay healing.

Comment: Sulfirgamide (M-dimethyl acroyl-sulfanilamide) as the sodium salt is quite soluble and stable in aqueous solution. It produces very little irritation of the eye, in 4 per cent to 15 per cent concentration when locally instilled and possesses a bacteriostatic and virostatic range similar to other sulfonamides.

IRVING H. LEOPOLD

THE UVEA

STUDIES ON THE ETIOLOGICAL PROBLEM OF UVEITIS

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Brit. J. Ophth., 1955, *39:* 545–556

Two hundred patients with uveitis were studied irrespective of their clinical classification and findings were analyzed in relation to the site of the lesion, namely, anterior, posterior or panuveitis. Anterior uveitis occurred more frequently in females than in males. Males showed an apparently earlier onset of posterior uveitis.

None of the 200 cases had a positive Wassermann or Kahn reaction. In only two cases was the gonococcal complement fixation test positive and in neither instance was a history of venereal disease obtained. It is regarded as unwise to regard the test as diagnostic in the absence of other evidence of the disease.

The results of the Mantoux test follow closely those to be expected in the population at large. A high cutaneous sensitivity appears to be more frequent in those patients with anterior than in those with posterior uveitis.

A normal blood count was the rule. No correlation could be found between uveitis and the hemoglobin level. Twelve white blood counts showed more than 12,000 white cells per cu.mm.; five occurred in anterior uveitis, one in posterior uveitis and six in total uveitis. Polymorphonuclear leukocytosis occurred in 13 patients and in 10 infection could be found: two with a positive gonococcal complement fixation test, three with staphylococcal infections, one with active pulmonary tuberculosis, one with Behcet's disease, one with laryngitis, one with septic teeth, one with active toxoplasmosis.

The results of the brucella agglutination test suggest that this infection is not etiologically significant in Great Britain. Serologic evidence of infection with toxoplasmosis was found in 43.9 per cent of these patients. In Great Britain, 25 per cent of the "normal population shows positive results and in all groups of uveitis, the incidence was above this figure, being most significantly raised in the posterior uveitis group (67.7 per cent). The authors feel that although the titer levels are not diagnostic in individual cases, they do show a striking association between toxoplasma infection and posterior uveitis.

A statistically significant relationship between elevated antistreptolysin titers and anterior uveitis was found. This supports previous studies, notably by Woods (Arch. Ophth., *52:* 174, 1954) suggesting that "nongranulomatous uveitis"—which is predominantly anterior—may not infrequently be due to an underlying streptococcal hypersensitivity.

It is clear that laboratory investigations gave little assistance in establishing the cause of the condition in individual cases. In not more than 10 per cent was a certain pathologic diagnosis established and in a large group, probably 40 to 50 per cent, there was no indication of the possible nature of the disease. When the findings were grouped, a striking association between streptococcal infection and anterior uveitis and between toxoplasma infection and posterior uveitis was revealed.

Comment: This is a most important contribution and is in keeping with the findings of many groups of investigators. The difficulty in finding an etiologic factor should not lead to a helpless resignation at the inability to find the cause of uveitis. Skin tests with tuberculin, toxoplasmin, coccidiodin, histioplasmin and brucellergin are helpful. A blood Kahn, agglutination for brucella, and dye test for toxoplasma (if available) should be done. The antistreptolysin titre is easily performed and should be done. Blood glucose, uric acid and albumin-globulin studies are helpful. The white blood count may suggest an infection somewhere in the body. Careful studies for focal infection are usually unrewarding; nonetheless, if only as a hygienic measure, infections in the sinuses, teeth, pharynx and genitourinary tract should be eradicated if possible.

The role of toxoplasmosis in ocular infection is most difficult to evaluate. The disease is ubiquitous and a large percentage of the "normal" population shows positive titers. Unless the titer is increasing or decreasing, it is impossible to draw conclusions concerning activity of the disease. Sabin has recently suggested (W. H. Wilder Lecture, Chicago, in press) that the organism may lodge in the eye in an encysted form and not give rise to ocular signs. At some later time, when all signs indicate quiescence of systemic disease, the cyst ruptures, liberating the organisms and causing disease. Thus there may be an active disease in the eye with no signs of systemic disease.

Sabin suggests that two or three hospitals in the United States be designated for toxoplasmosis research and all eyes to be enucleated because of uveitis be channelled to these centers. At the time of enucleation a trained parasitologist could do appropriate animal inoculations to learn if these eyes harbored the parasite. Such studies correlated with dye tests and complement fixation studies would do much to indicate the importance of toxoplasmosis in ocular infection and the significance of blood tests.

Basic Sciences

ANATOMY

ANATOMIC AND PHYSIOLOGIC ASPECTS OF THE CAPILLARY BED IN THE BULBAR CONJUNCTIVA OF MAN IN HEALTH AND DISEASE

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Angiology, 1955, *6:* 369–382

Earlier studies of the capillary bed in living humans were directed primarily at the blood supply of the nail fold in the fingers and toes. Information available from examination of the vessels in these areas, however, is limited by the lack of a complete capillary network with its various elements and by the overlying epidermis which interferes with clarity at high magnification. The author observed that topography of the vascular bed in the conjunctiva compared very favorably with that in the mesenteric region of living small laboratory animals.

The bulbar conjunctiva of man was studied with a Poser slit lamp and with a dissecting microscope with accessory light source. Magnifications higher than 100× are not satisfactory in man because of the fine, automatic, oscillatory movements of the eye ball not under volitional control of the subject. This results in vessels moving rapidly in and out of the field of view. In the supine position ballisto-cardiac phenomena were clearly observed and accurate photomicrography was almost impossible at high magnification.

In the normal capillary bed the heavy prominent dark vessels are collecting venules which are paralleled by narrower, straighter vessels comprising the accompanying terminal arterioles. From these arterioles small metarterioles arise and then send off true capillary side-branches. These, in turn, unit to form the finer radicles of the collecting venules.

Epinephrine (1:50,000) caused a complete disappearance of the capillaries because of closure of pre-capillary sphincters. The arteriole and venule changed but slightly in diameter. Prolonged exposure to traumatic stimuli such as a heavy wind, extreme cold or heat produced vasodilation in the conjunctival vessels particularly on the venular side of the capillary bed. These changes can be readily detected because of the absence of spontaneous vasomotor activity, reduced velocity of flow, and overall increase in arteriolar and venular diameters.

In the menstrual cycle during the period 8 to 5 days premenstrually there is

a prominent vasoconstriction, an increase in spontaneous vasomotor activity in the capillary bed, and tissue ischemia. At the onset of menstruation, or just prior, these changes are replaced by fairly sudden arterial dilation, a reduced blood flow or velocity and, not uncommonly, small venular petechiae. Cyclic changes in the capillary bed persist through the first trimester of pregnancy.

In hypertensive disease there is a pronounced degree of elongation, looping, coiling, and "corkscrewing" in the true capillaries and collecting venular system. These changes are associated with narrowing of the terminal arterioles and an augmentation of responsiveness to topical epinephrine. The velocity of blood flow is reduced and the number of red cells passing through a patent capillary may be reduced by 50 per cent.

The mean speed of blood flow in the human terminal arteriole has been determined to be 100 microns per second. In the true capillaries it averages about 26 microns per second and in a collecting venule speeds to about 56 microns per second. If the average velocity in the capillary falls below 10 to 15 microns per second the red cells tend to form small aggregations described as "granular flow." This may be induced in any individual by the application of heat or cold, or any pharmacologic stimulus that reduces the velocity of capillary blood flow.

In patients with an increased capillary fragility as determined by the tourniquet test, unusual saccular and fusiform dilations in the venules are present. A profound terminal arteriolar and venular dilation accompanies vascular headache, on the same side as the headache.

It is concluded that a single criterion of peripheral vascular abnormality such as follow response to a drug, change in velocity of blood flow or anatomic variation are not specific for the diseased state.

Comment: Edmund P. Fowler, Jr., Professor of Otolaryngology at Columbia University, in his discussion of this paper, described in detail some of the difficulties encountered in interpretation of the appearance of the conjunctival capillary bed. The major problem is the discrimination between the normal and the abnormal. At least three vascular modifications are probably not pathologic for given individuals: first, slow flow which is common near the lids; second, appearance of vessels larger than conventional capillaries; and third, decreased superficial and deep circulation.

One of the surprising aspects of the study of the conjunctival capillary bed is the minimal interest of the ophthalmologist. The majority of studies concerning this interesting field has originated with clinicians in widely divergent fields. Much of this lack of ophthalmic interest probably originates with the many abnormal vascular patterns observed daily in practice and associated with local ocular disease. When these findings are combined with those which arise because of systemic disease and those secondary to local traumatic stimuli the ophthalmalogist despairs of ever distinguishing between normal and abnormal.

Difficult as such a study would be, it would seem that the logical group for evaluation of the normal would be healthy children just before puberty. Since their conjunctiva is usually much clearer of blood vessels than the adult, it is suspected that many of the blood vessels visible in the adult are the result of repeated traumatic stimuli from normal exposure to years of wind, smoke and infection. These vessels, of course, constitute a true capillary bed but one which varies considerably from individual to individual and, as the author has shown, one that reacts in a similar manner not only to systemic disease but to cyclic physiologic variations of the body and to mild external trauma.

BACTERIOLOGY

VARIATIONS IN MORAX-AXENFELD DIPLOBACILLUS

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A. M. A. Arch. Ophth., 1955, *54:* 580–585

When a culture of Morax-Axenfeld bacillus was left out for five days it was noted that the microscopic appearance of the organisms changed. The bacteria became much shorter and tended to lose their Gram-negative staining characteristic. Additionally, they tended to retain these new characteristics on subsequent blood-agar transfers.

Because of the frequent finding of an unidentified Gram-positive diplobacillus in smears of Morax-Axenfeld conjunctivitis studies were directed toward elucidation of variant forms of the Morax-Axenfeld diplobacillus.

It was apparent that continued culture on blood agar encouraged the development of the Gram-positive micrococcal form and continued culture on liquid media encouraged the development of the Gram-negative diplobacillary form. Continued manipulation could make the organism take on either appearance, as desired. Not only was there a marked variety in form, but the specimens ran the whole gamut of color, varying from an almost invisible pale pink to an intense dark blue. In some cultures capsules could be seen; in others, bloated forms; some liquid cultures produced long, coiled filaments, and in still others one could see cocci and bacilli in the same field, or Gram-posiive and Gram-negative forms in the same field. To be certain that none of this was due to contamination or error, an added precaution was taken. On the appearance of a different form, either morphologically or in staining quality, the organism was cultured back to the preceding color and shape by the use of appropriate media.

It is apparent, then, that remarkable variations in morphology, cultural characteristics, and biologic behavior can occur in certain bacteria. Quite possibly it has been failure to recognize these potentialities that has caused confusion in our clinical and bacteriologic approach. It must be realized that the bacterium can masquerade under various guises, depending more or less upon the materials at hand, and can perform a versatile repertoire of noxious acts, depending more or less upon the opportunities at hand. Awareness of this can reduce the numbers of organisms in classifications and can account for different clinical pictures caused by one organsm. It is easier to believe that the same organism can cause both hypopyon keratitis and angular conjunctivitis, and that the classical differentiation into the Morax-Axenfeld bacillus and the diplobacillus of Petit is

unnecessary. Also, in Mitsui's experiment we can now consider the possibility that micrococci did not develop spontaneously in the conjunctival sac, but that they developed from Gram-negative diplobacilli placed there.

Comment: Variations in morphology are seen with some regularity in Gram-negative species. For example, the influenza bacillus, appearing as rods in conjunctival secretions, assumes a cocco-bacillary form in culture. Loss of Gram-positiveness is common in old cultures and those grown under unfavorable circumstances. On the other hand, a change from Gram-negative to Gram-positive would be most unusual in the course of normal growth.

In a recent conversation, Drs. Mitsui and Tanaka confirmed their belief that the micrococcus recovered by them was a separate symbiotic organism and not a variant of the diplobacillus nor of the diphtheroid group. It is, however, interesting to note in this connection that diphtheroids undergoing degeneration resemble Gram-positive cocci on occasion.

The present study should stimulate further investigation of the strain used by the authors. The demonstration of immunologic identity of the presumed variants would strengthen their case.

HENRY F. ALLEN

CHEMISTRY

SODIUM AND CHLORIDE OF THE AQUEOUS HUMOR OF NORMAL AND SCORBUTIC GUINEA PIGS

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Brit. J. Ophth., 1955, *39:* 534–538

The steady state ratio of the concentration of sodium and of chloride in the aqueous humor to that of the plasma was studied in normal, scorbutic and ascorbic acid saturated guinea pigs. Scholz demonstrated that in the scorbutic guinea pig there was a fall in aqueous humor sodium, suggesting that ascorbic acid was essential for the secretion of sodium into the aqueous from the plasma. Ridge suggests that to maintain electrical neutrality with the decrease in sodium concentration there must be either an entrance of an equivalent decrease in anion, or compensatory changes in both. Entrance of other cations would profoundly alter the character of the blood aqueous barrier and it seemed that any alteration would involve the anion concentration, most likely the chloride ion.

Compensatory change in the chloride concentration was not found. In the present experiments no difference could be found in the aqueous-plasma distribution in normal and scorbutic guinea pigs. The chief difference in the techniques of the present author and Scholz was the much less severe scorbutic state of the animals in this study. Two possibilities are suggested by this study: (1) that ascorbic acid may be involved in the maintenance of the potential difference between the ciliary epithelium and stroma, but that the transfer of sodium across the blood-aqueous barrier is not dependent on this mechanism, and (2) that the transfer of sodium is related to the potential difference, but that ascorbic acid plays no part in its maintenance.

Comment: Since the original presentation of Friedenwald's theory of aqueous formation (Arch. Ophth., 1938, *20:* 761) there have been practically no experiments reported that could not be fitted into the hypothesis. This has been particularly true of the work of Kinsey on aqueous flow (Am. J. Ophth., 1949, *32:* 177 and Arch. Ophth., 1950, *44:* 215); and of Becker on inhibition of aqueous flow by Diamox (Am. J. Ophth., 1954, *37:* 13). Indeed a brilliant episode in the treatment of glaucoma was thus introduced on the basis of Friedenwald's concept. An outstanding exception to this was the paper by Barany in 1951 (Arch. Ophth., 1951, *46:* 326). He failed to show any change in aqueous production in ascorbic acid deficient animals and this work is borne out by that of Ridge who fails to demonstrate a change in the concentration of sodium (and chloride) in the scorbutic guinea pig. One would normally expect a decrease in both total flow and in sodium concentration if the production of aqueous by the ciliary body were dependent on the presence

of ascorbic acid. A basis for reconciliation of his results with previous data is succinctly summarized by Ridge in the last two paragraphs of his discussion.

DAVID SHOCH

CARBOHYDRATE METABOLISM OF LENS

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A. M. A. Arch. Ophth., 1955, *54:* 360–368

It has been generally assumed that the glucose metabolism in the lens is similar to that which predominates in other tissues. In most mammalian tissues, glucose is catabolized first anaerobically to lactic acid by a process known as the glycolytic pathway and thence aerobically to carbon dioxide by a process known as the citric acid cycle. But the peculiar avascularity of the lens and its low oxygen consumption do not allow one to make any *a priori* assumptions as to the utilization of glucose by the lens. It is known that oxygen is essential for the maintenance of the viability of the lens, but heretofore no study has been made of pathways in the lens other than the classical types referred to above.

Studies with radioactive carbon indicated that the citric acid cycle is relatively inactive in the lens. Studies of enzymes present in the lens indicate that the pattern of the aerobic phase of glucose metabolism is different in the lens than in other tissues. The results indicate that in the lens the direct oxidative pathway accounts for most of the carbon dioxide produced from glucose.

It is possible in the lens that in place of the cytochrome system, the glutathione-ascorbic acid oxidative mechanism is effective. In this mechanism the oxidation of reduced triphosphopyridine (TPNH) by oxidized glutathione is catalyzed by glutathione reductose. There is suggestive evidence that dehydroascorbic acid oxidizes glutathione, although it is not known whether the reaction is mediated by an enzyme. The conversion of ascorbic acid to dehydroascorbic acid has not been demonstrated. Perhaps *in situ* the lens utilizes the dehydroascorbate furnished by the aqueous humor.

Comment: This paper is one of the most exciting and fundamental pieces of work ever done on the lens. Although our knowledge of lens metabolism has increased greatly in recent years, the work in this field has by and large been postulated on the thesis that the metabolism of the lens follows the pathways elucidated for other tissues, primarily muscle. In large part this has been found to be true, but there have been many discrepancies. For example, a major component of enzyme systems in other tissues are the cytochromes.

At first these were thought to be absent in the lens; later Kinsey showed that these co-enzymes were present in the lens epithelium. In most tissues, however, these co-enzymes exist in the mitochondria, a structure conspicuously absent in lens fibers. Secondly, the large excesses of ascorbic acid and glutathione in the lens have been an embarrassment to the investigator with a belief in the essential economy and orderliness of the body. Dr. Kinoshita, in showing that the citric acid cycle is unnecessary to the metabolism of the lens, has provided the long sought for answers. Apparently the essential co-enzyme in the lens is TPN (triphosphopyridine nucleotide) which is kept in the oxidized state by giving its hydrogen to oxidized glutathione. Furthermore, since in contrast to the cytochrome system, TPN and glutathione exist outside the mitochondria, this eliminates the need for opaque little bodies in the cell cytoplasm. What a wonderful asset to a structure whose primary function is transparency! A final and most important implication of Dr. Kinoshita's work is that it opens a whole new area to be investigated by those interested in the pathogenesis of cataract formation.

DAVID SHOCH

COLOR VISION

A SIGN OF MANIFEST HETEROZYGOSITY IN CARRIERS OF COLOR DEFICIENCY

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Am. J. Optom.; Arch. Am. Acad. Optom., 1955, *32:* 404–408

Congenital red-green deficiency is transmitted by the sex chromosomes which are designated by XY in the male and by XX in the female. With the male only the one X chromosome has to be affected in order to cause color deficiency but in the female both X chromosomes must be affected before color defect is produced. Where only one of the X chromosomes is affected in the female, she will be a carrier. A woman may be color defective when her father is color defective and her mother either a carrier or a color defective.

There has been some evidence that the normality gene of heterozygotes is imperfectly dominant and that the genes in non-allelic compounds do not neutralize each other.

The following results were based on the investigation of 35 carriers: 7 for protanomaly, 6 for protanopia, 17 for deuteranomaly and 5 for deuteranopia. They were most probably normal-color defective heterozygotes, their type being defined by their color deficient sons. All 35 carriers passed color vision chart tests. On the anomaloscope some of them showed enlargement of their matching range, the average being normal. Most carriers of protoforms have their average settings between the normal mean and the normal limit toward protanomaly and the carriers of deuteroforms have their average settings between the normal mean and the normal limit toward deuteranomaly.

Measuring the luminosity curve of a carrier for protanomaly showed an intermediate course between that of normals and that of protanopes. The luminosity curves of nine other carriers of protoforms showed a similar deviation with slight individual differences which, however, did not allow a discrimination of a carrier of protanomaly from that of protanopia. The luminosity curves of nine carriers of deuteroforms coincided with that of a normal person.

The shift of the luminosity curve of protoform-heterozygotes implies that the gene for color deficiency is incompletely recessive. The result is a contribution to the theoretical concept about color vision since it suggests that brightness and chromaticness must be mediated independently in the visual system. The detection of carrier is not only of theoretical but also of practical interest because carriers should be excluded from serving as experimental subjects in any research work on normal color vision.

Comment: This paper reaffirms a discovery made in 1934 and neglected since: that a woman who "carries" red-blindness (protanopia or protanomaly) can be easily identified from her abnormal brightness vision although her color vision is normal. Asked to match the brightnesses of a fixed green light and a variable red one, she will require excessive voltage on the red lamp. The phenomenon is one of many that suggest that brightness and coloredness are to some extent distinct in physiologic mediation.

If Mary's father is red-blind, Mary is a carrier and half of her sons will be red-blind. But with a normal father, Mary may be a carrier if her mother is one. The depression of red-light brightness, "Schmidt's sign," clinches the matter if it is present. Not every protanoid carrier exhibits it at a given time. There are recent indications that this is because the depression is not stable but slowly comes and goes. This would emphasize the physiologic nature of the basis of Schmidt's sign, whereas red-blindness itself probably has a structural basis in the retina.

Schmidt errs in stating, twice, that in a double carrier of two color defects the defective genes can neutralize each other. If a double carrier is normal, it is because each defective gene is suppressed by a normality gene in the paired chromosome.

GORDON L. WALLS

OPTICS

SOME DIRECT COMPARISONS BETWEEN LIGHT AND DARK ADAPTATION

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J. Optical Soc. Am., 1955, *45:* 839–844

Light adaptation and dark adaptation are usually thought of as two opposite processes which serve to adjust a subject's visual sensitivity to the luminance level available at the moment. Dark adaptation is the increase in his visual sensitivity as the subject remains in the dark, and light adaptation is the decrease in sensitivity as he is exposed to light.

The point of view that light and dark adaptation are complementary changes is not always supported by the data from which the sensitivity changes are inferred, however, The difficulty lies in the fact that several techniques are available for measuring the course of the adaptation processes.

If the absolute threshold is used to trace the course of light adaptation, sensitivity appears to decrease regularly in the expected manner. On the other hand, if sensitivity is measured by means of the difference threshold, sensitivity appears to be poor at first during the process of light adaptation. It increases for a time, passes a maximum, then decreases to a final level.

The data were taken with three different devices. The measure of sensitivity in all cases was the threshold retinal illuminance of a round white stimulus spot subtending one degree of visual angle. When the stimulus was presented in the dark, it yielded an absolute threshold. When presented against an illuminated background, it yielded a difference threshold.

In the several experiments, the stimulus spot appeared both in the fovea and in the parafovea. Retinal position was controlled by means of fixation markers.

Fluctuations in the visual entrance pupil were avoided by using a small artificial pupil, and the data are reported in units of the troland to imply this control. The small artificial pupil and the brief duration of the stimulus resulted in thresholds which appear rather high. They are quite consistent with other measurements, however, when allowance is made for the stimulus duration and the pupil restriction.

According to photochemical theory, changes in the absolute threshold during dark adaptation reflect the accumulation of photosensitive materials in the retina, either in the simple manner in which rhodopsin accumulates in solution, or in some more complex way. Both the difference threshold and the absolute threshold are limited by photochemical conditions, when the eye is completely adapted to various luminances. We expect, therefore, that the difference threshold will behave similarly to the absolute threshold while the eye is dark adapting.

In the case of the absolute threshold, the process has been identified with the accumulation of photochemical substances in the visual receptor. The behavior of the difference threshold seems consistent with the same interpretation. Whether it is measured by absolute threshold changes or by difference threshold changes, dark adaptation appears well described as a reflection of photochemical changes.

In view of the success of the photochemical explanation in the case of dark adaptation, it might well be expected to apply to the opposite case of light adaptation. Since light adaptation is supposed to be due to the bleaching of photochemical materials, reducing the sensitivity, the threshold should begin low during early light adaptation, then rise to a final, higher level after complete adaptation. The threshold is low at first, showing high sensitivity, but the threshold rises continuously as sensitivity declines with the bleaching of photosensitive material in the adapting light. The absolute threshold clearly behaves as if it were limited by the bleaching of photosensitive materials during light adaptation.

The difference threshold, however, differs from the absolute light threshold during light adaptation, and does not reflect photochemical conditions. Further experiments suggest that in early light adaptation the difference threshold is limited not only by the photochemical balance in the receptor but by the ability of the receptor to discharge at high rates.

It is considered that the difference threshold is limited by the availability of responding units. Thus photochemical bleaching slows the discharge rate of the receptor until it can give an additional response more readily.

Comment: These are very beautiful experiments. They prove that during the dark- or light-adaptation process differential threshold and absolute threshold changes do not run similar courses. Hecht's photochemical theory might offer a satisfactory explanation for the changes of absolute threshold during dark- and light-adaptation (although even here it is too simple to explain all the complexities of these processes). It certainly offers no usable working hypothesis for the explanation of differential sensitivity. The author feels that, with some modifications, his curves of differential sensitivity can be made to fit those of absolute sensitivity. It is questionable that anything is gained by such forced conformity. The author's experimental results certainly deserve to be studied on their own merit and should lead toward a satisfactory theory of differential sensitivity.

ARTHUR LINKSZ

A QUANTITATIVE TEST FOR DETERMINING THE VISIBILITY OF THE HAIDINGER BRUSHES: CLINICAL APPLICATIONS

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Am. J. Ophth., 1955, *40:* 393–405

In plane polarized light the normal eye can see an entopic pattern consisting of two tufts which radiate in opposite directions from the fixation point. The phenomenon depends entirely upon regional variations in the brightness of the blue component of the incident light. The pattern is, therefore, most easily seen in such light where it appears as a dark figure on a blue background. In white light the two brushes are yellow. The brush phenomenon tends to fall rapidly if a fixed region of the retina is stimulated. If the pattern is caused to rotate by continuous rotation of the polarizer, practically all normal eyes can see the dark brushes formed in blue light.

By means of filters the authors studied the lowest luminance at which the direction of rotation of the brushes could be reported correctly.

The Haidinger brushes were subnormal in the great majority of the eyes having macular disease. Low scores were also noted in eyes with various forms of optic neuropathy, but only if visual perception was impaired in a major portion of the central field in which the brushes would normally appear.

In high degrees of amblyopia ex anopsia with vision of 20/100 or less, the Haidinger brush scores were normal in some instances, markedly reduced in others. The ability of the amblyopic eye to perceive the brush pattern probably depends primarily upon the extent of the central area in which function is depressed in monocular vision.

Subnormal brush scores were sometimes noted as a result of a cataract or an advanced keratoconus. The reduction in visibility of the entoptic pattern by such defects of the ocular media is probably the result of scattering, absorption, and partial depolarization of the incident light.

Seven subjects whose eyes were apparently free of any form of ocular disease saw either no brush pattern whatsoever or a very incomplete form of the normal pattern. Other findings suggest that some congenital anomaly of the macular structures was responsible for the absence of the normal entoptic pattern.

Because of the many different causes of subnormal Haidinger brush scores, the test is of only limited value in differential diagnosis. A markedly subnormal brush score in association with a minimal field defect is however strongly suggestive of a macular rather than an optic nerve lesion. Central serous retinitis in particular can be associated with an obviously subnormal Haidinger brush score at a stage at which the condition could easily be overlooked on routine examination. In a cataractous eye with low vision, a normal score can be considered as reliable evidence of an intact macula.

The chief merits of this new test as a supplement to standard procedures are

(1) it is rapid and simple; (2) it is not influenced by uncorrected ametropia, and (3) it gives reliable results in patients whose unsteady fixation interferes with detection of a central field defect.

Comment: It was more than a hundred years ago that Haidinger's brushes were discovered, still only lately has it turned out that the phenomenon might have clinical significance. This is, first of all, due to Goldschmidt's studies.

The present investigation is of interest in two respects: It offers a standardized quantitative test and an easily readable score of the visibility of the brushes; secondly, it enlarges the scope of the clinical material. One learns that ". . . perception of the brushes is likely to show greater impairment in macular than in postretinal lesions with equal impairment of visual acuity." These findings certainly do not contradict Goldschmidt's view, although the authors think they do.

Significant is the extension of the investigation upon a group of congenital anomalies (night blindness, monochromatism, etc.) and cataract. It is somewhat disappointing to find that the problem of amblyopia ex anopsia has not been studied in greater detail. Of 12 amblyopes with 20/100 visual acuity or less, six had negative scores while five showed normal scores. In spite of equally low visual acuity, these may be two entirely different types of amblyopia. Goldschmidt's contention that the latter group is amenable to treatment needs urgent critical reappraisal on larger material. Confirmation by the new, more accurate, quantitative test would be of immense prognostic significance for the orthoptic laboratory.

ARTHUR LINKSZ

EFFECT OF REFERENCE LINES ON THE DISCRIMINATION OF MOVEMENT

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J. Optical Soc. Am., 195,5 *45:* 829–830

Motion may be "perceived" directly at intermediate target velocities or "inferred" from observation of change of position at slower speeds. The present experiments were to test the hypothesis that the presence of reference lines should lower the threshold velocity at long but not at short exposure durations.

The minimum discriminable target velocity was determined with and without reference lines in the visual field. At a short (0.125 sec.) exposure duration, where velocity discrimination is determined primarily by the magnitude of initial photochemical events, the velocity threshold is not changed by the introduction of reference lines. At a long (16 sec.) exposure duration, the presence of reference lines lowers the threshold velocity by 48 per cent. The data are interpreted as supporting the hypothesis that movement is discriminated at slow speeds by observation of change of position.

Comment: The experiments are well executed and confirm what Exner (1875) already pointed out, viz. that motion can be perceived directly or inferred by change of relative position. Some new knowledge is, however, added and one of the least clarified psychophysiologic phenomena, the discrimination of movement, should now become better understood.

ARTHUR LINKSZ

EFFECT OF DIFFERENTIAL ADAPTATION OF THE EYES UPON THRESHOLD SENSITIVITY

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J. Optical Soc. Am., 1955, *45:* 831–834

The independence of the states of adaptation of the two eyes is so generally accepted that it is stated in secondary sources without reference to experimental basis. However, experimental evidence against such a belief does exist. Cook (Psych. Mon., 1934, *45:* 3) reported that foveal thresholds in the earlier stages of dark adaptation were lower after binocular adaptation than they were if only the tested eye were light-adapted. Elsberg and Spotnitz (Bull. Neurol. Inst. N.Y., 1938, *7:* 148) found that briefly light-adapting one eye depressed foveal sensitivity in the other and that recovery time was a positive function of the adapting luminance.

The present experiment was selected as the most likely to detect a binocular effect if one existed. To make the test as sensitive as possible the adaptation discrepancy between the eyes was maximized by maintaining the tested eye in a fully dark-adapted state, and using the highest obtainable luminance as the light-adapting stimulus for the other eyes. The threshold in the right eye with both eyes dark-adapted was compared to course of the threshold in the right eye immediately after the left eye had been adapted to a high luminance level.

Statistical analysis indicated that variances occurring were not large enough to indicate that any interocular effect had occurred. It was thus concluded that adapting one eye to a very high luminance level does not decrease the immediate light sensitivity of the other dark adapted eye. It is thus unnecessary, under these conditions, to hypothesize a central adaptation process.

Comment: With some contradictory experimental results existing, one will be glad to have in this paper what seems to be good proof of experimental evidence. One will thus accept as proven (1) that light adaptation of one eye does not influence the sensitivity of the other, and (2) that there is no need to hypothesize a central adaptation process.

ARTHUR LINKSZ

PHYSIOLOGY

TWO TYPES OF OCULAR MOTILITY OCCURRING IN SLEEP

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J. Appl. Physiol., 1955, *8:* 1–10

Eye movements during sleep were studied by means of electro-oculograms and direct observation in 26 adults and 1 child, all of whom were presumably normal and in good health. Simultaneously, records were made of electroencephalographic activity and the respiratory rate, heart rate, and body motility. Two distinct types of movements were found: (1) a slow lateral movement similar to that seen in sleeping infants and in adults during sleep and anesthesia, referred to as slow eye movement, and (2) a new type of ocular motility, characterized by rapid, jerky motions of relatively short arc, referred to as rapid eye movement. The slow eye movements were seen at the onset of sleep and together with and after every body movement throughout sleep. The frequency of these movements declined gradually after each body movement; several times during the night, especially when delta waves were evident, they were not discernible. The mean duration of the periods of complete ocular quiescence was 24 minutes 55 seconds. The rapid eye movements were binocularly synchronous and appeared in clusters of about 20 minutes' duration. The first cluster appeared from 1 to 5 hours (3-hour average) after retiring, a second cluster about 2 hours later, followed by additional groups of eye movements at still closer intervals depending on the length of sleep. The appearance of the rapid eye movements was accompanied by a statistically significant increase in heart rate (10 per cent average) and respiratory rate (20 per cent average), a typical low voltage electroencephalographic pattern from the frontal and occipital areas, increased bodily activity, including facial movements, and occasionally vocalization. Evidence obtained by interrogation of the subjects, supported by other indications, led to the conclusion that the rapid eye movements were involved in the visual imagery accompanying dreaming.

Comment: These investigators employ one of the newer methods of recording eye movements which interferes minimally with ongoing behavior of the subject. Elsewhere they report data on infants under 7 months of age. Sleeping infants gave only the slow, pendular, binocularly asymmetrical type of eye movement. These occurred in episodes between periods of quiescence, and were associated with peaks in underlying cycles of general bodily activity, as are the bursts of both types of eye movement found in sleeping adults.

The authors show due caution in drawing conclusions about cause and effect, placing emphasis on correlations. One interpretation of the slow eye movement is that this represents functions from strictly subcortical innervation. The jerky synchronous movement is regarded as a fixation type of eye movement where cortex is active (as represented by low voltage EEG patterns and reports of dreaming). The approach promises further usefulness in the study of normal and anomalous development of motility patterns.

Austin Riesen

PHYSIOLOGY OF VISION

VISUAL PATTERN PERCEPTION FOLLOWING SUBPIAL SLICING AND TANTALUM WIRE IMPLANTATIONS IN THE VISUAL CORTEX

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J. Comp. & Physiol. Psychol., 1955, *48:* 50–58

The importance of transcortical intragriseal conduction in visual pattern perception was tested in seven cats. The animals, which were one-half to three-fourths grown at the start, were trained to select an equilateral triangle when it was paired with various ones in a series of other imperfect triangular patterns of the same dimensions. They were trained to a criterion of 17 correct out of 20 consecutive trials on all the negative figures with which they were to be tested after having been subjected to subpial slicing and tantalum wire implantation in the visual cortex. The operations were performed aseptically, with the animals under sodium pentobarbital anesthesia. The knife cuts intersected one another in criss-cross patterns, extending through the depth of the grey matter and invading the white matter; the wires, used in four cases, were inserted in random patterns throughout the visual area and the subjacent white matter. Ten days at least were usually allowed for recovery from the operation and then the animals were retested on the various patterns. Finally, post-mortem records and studies were made of the brains of the cats after they had been given a lethal dose of sodium pentobarbital. A generally high level of performanee was shown by the animals in the postoperative tests. No marked disturbance of visual pattern perception was produced by either the extensive subpial slicing of the entire visual cortex or its dense impregnation with metallic wires. The absence of a generalized functional breakdown speaks against transcortical intragriseal conduction, including direct current flow, as an important factor in perceptual organization, i.e., in dimensions that might mediate relational effects in form perception. The stimulus figures were too large to have been projected in most cases into intact cortical tissue between the wires or the knife cuts. Furthermore, after operation as well as before, the cats approached the figures more closely—instead of the reverse—as their difficulty increased. Not uncommonly the animals operated on approached the negative figures of all series so closely that the projected retinal patterns must have extended over roughly one-half to two-thirds the entire visual cortex. The findings in cases in which there were large bilateral lesions in the tectum discount the possibility that the superior colliculi, or the visual area of the cerebellum to which they relay, might have served as substitute centers for the cortical organization. The bordering visual "association" area of

the cortex also seems to be ruled out by the extension of the cuts and the wires into this region. No abnormalities in visuomotor coordination that could be attributed to the cortical knife cuts or the implanted wires were noted at three weeks after operation in casual observations of the cats' ability to jump, to walk a narrow board, or to follow and catch rapidly moving small objects.

Since ordinary fiber conduction is permanently blocked by subpial knife cuts, the results obtained in these experiments are difficult to reconcile with theories of perception based on reduplicated interference patterns or on the alpha rhythm as a scanning device; at present, they seem to favor a more vertically organized, motor-conditioned concept of cerebral integration.

INTEROCULAR TRANSFER OF LEARNING IN VISUALLY NAIVE AND EXPERIENCED INFANT CHIMPANZEES

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Yerkes Laboratories of Primate Biology and Yale University, New Haven, Connecticut

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The significance of early visual experiences for the perceptual equivalence of the two eyes in a higher primate having an anatomical basis for binocular fusion has been elucidated by the study of infant chimpanzees.

In higher primates some fibers of the optic nerve cross at the chiasma to the contralateral cerebral hemisphere and some remain on the ipsilateral side. The number of crossed and uncrossed fibers is estimated to be about equal in monkey and in man, and this probably also holds for the chimpanzee. Fibers from the corresponding parts of the two retinas make synapses at the lateral geniculate body, and these fibers terminate together at the striate cortex. The two lateral geniculates have no known interconnections; they probably serve only as relay stations. The existence of direct pathways from one cortical visual area to the other also has yet to be clearly demonstrated. These anatomic considerations suggest that the functional equivalence of the two eyes—i.e., the fact that the world looks the same to us through either eye alone, and that an untrained human adult eye mediates visual tasks learned monocularly through the other eye—probably is not determined solely by innate organization between either the two geniculates or the two striate areas.

Previous studies on interocular transfer of visual habits in various animals had indicated the importance of both structural and experiential factors. Thus it was found that cats reared in darkness and then given patterned light to one eye and diffused light to the other do not immediately transfer visual discrimination learned with the eye receiving the patterned light to the other. (By "patterned

light" is meant that provided by an ordinary, lighted room environment, including forms, colors, shadings, and movements of the subject and of objects in the room. "Diffused light" is homogeneous, nearly white light with no contours or movements.) They acquire the habits with the diffused-light eye, however, with a large amount of saving. This suggests that, in spite of the anatomic convergence of the optic fibers from two retinas to the same visual area, complete functional equivalence of the two eyes is not assured without some patterned-light experience.

The present study was undertaken to determine the occurrence of interocular transfer of visual habits in infant chimpanzees reared under varying conditions of light stimulation: (1) monocular light stimulation, one eye with patterned light, the other eye with diffused light only; (2) monocular patterned-light stimulation; (3) binocular patterned-light stimulation. After visual discrimination habits were learned with one eye, the ability to perform these habits with the other eye was tested.

Six infant chimpanzees born at the Yerkes Laboratories were separated from their mothers within 28 hours after birth and were reared in the nursery under standard conditions of diet and care. Two controls had normal, binocular patterned-light experience. One subject (Margo) was kept in total darkness except that one eye at a time was exposed to patterned light, each for 1.5 hr. per day. The three experimental subjects (Laru, Sally and Norma) were also kept in total darkness, but one eye was exposed to patterned light, the other to diffused light, each for 1.5 hr. per day. All infants were trained on visual discrimination problems with one eye and were tested for interocular transfer to the other eye.

(1) The two normal controls learned to discriminate horizontal versus vertical striations with the right eye and showed immediate interocular transfer of this habit to the left eye.

(2) Margo learned the horizontal versus vertical striations with one eye and a red versus blue habit with the other eye concurrently. She showed perfect interocular transfer of both habits.

(3) Laru and Sally were trained on three discriminations in succession. Laru learned the first two habits with her patterned-light eye and the third habit with her diffused-light eye. Sally learned the first and third habits with the diffused-light eye, the second habit with the patterned-light eye. Norma was trained on two problems, each to one eye, concurrently. These animals showed no immediate interocular transfer on any of the habits, but relearned them with much saving.

The lack of immediate interocular transfer in the last three subjects is attributed to a central mechanism rather than to peripheral factors. It is suggested that the functional equivalence of the two eyes in infant chimpanzees is not determined by the structure of the central visual system alone. The anatomic overlap of optic fibers from the two retinas to the same cortical areas is initially incomplete and not adequate for interocular transfer. Some patterned-light experiences, either binocular or monocular, are needed to achieve complete functional interocular equivalence.

Comment: The study by Sperry and coauthors is further evidence against the theory that visual patterns are perceived by virtue of electrical fields or "maps" of the seen world projected to the cortex. Discrete fiber connections leading away from the projection areas are the alternative routes for perceptual integration. Neuropsychologists conceive of complicated networks of sensory-motor and nonspecific cortical loops, amplified from primitive pathways by a process of association, to explain the interaction between sensory mechanisms of vision and visually guided behavior. Animal experiments which have prevented exposure to visual patterns in early infancy are measuring the extent of deficit in visual performance that results when the "conditioned" pathways are not permitted to develop. According to the study by Chow and Nissen, even the interconnections for the normal equivalence of the two eyes in pattern recognition are not fully provided by embryonic growth or maturation. Some form of modification or sensitization by use is necessary. Opportunity to respond to visual patterns must apparently be fairly extensive and extended in time. Research is needed to answer the more detailed questions concerning kinds of interaction between visual stimulation, optomotor and gross motor activities that will assure the development of fully coordinated visual functions.

In their chimpanzee subjects Chow and Nissen found inadequacies of binocular reflexes, fixation anomalies, and late development of the protective eyeblink. All of these findings tend to confirm the need for early usage. Binocular exposure to visual patterns is a necessary (albeit not always sufficient) condition for normal development. These chimpanzee experiments tend to confirm, through the data reported, a conclusion stated in C. A. Worth's *Squint* (1939): "The orientation and vergence reflexes are present in rudiment at birth; but these rudiments, if not early used, are lost. Their preservation, and the whole of the rest of their development, are conditioned by usage."

AUSTIN RIESEN

Classics of Ophthalmology
JAMES E. LEBENSOHN, Editor

EXTRAORDINARY FACTS RELATING TO THE VISION OF COLORS

JOHN DALTON

Memoirs of the Literary and Philosophical Society of Manchester, 1798, *5(pt. 1)*: 28

Read October 31st, 1794

It will scarcely be supposed, that any two objects, which are every day before us, should appear hardly distinguishable to one person, and very different to another, without the circumstance immediately suggesting a difference in their faculties of vision; yet such is the fact, not only with regard to myself, but to many others also, as will appear in the following account.

I was always of the opinion, though I might not often mention it, that several colors were injudiciously named. The term pink, in reference to the flower of that name, seemed proper enough; but when the term red was substituted for pink, I thought it highly improper; it should have been blue, in my apprehension, as pink and blue appear to me very nearly allied; whilst pink and red have scarcely any relation.

In the course of my application to the sciences, that of optics necessarily claimed attention; and I became pretty well acquainted with the theory of light and colours before I was apprized of any peculiarity in my vision. I had not, however, attended much to the practical discrimination of colours, owing, in some degree, to what I conceived to be a perplexity in their nomenclature. Since the year 1790, the occasional study of botany obligated me to attend more to colours than before. With respect to colours that were white, yellow, or green, I readily assented to the appropriate term. Blue, purple, pink, and crimson appeared rather less distinguishable; being, according to my idea, all referable to blue. I have often seriously asked a person whether a flower was blue or pink, but was generally considered to be in jest. Notwithstanding this, I was never convinced of a peculiarity in my vision, till I accidentally observed the colour of the flower of the Geranium zonale by candle-light, in the Autumn of 1792. The flower was pink, but it appeared to me almost an exact sky-blue by day; in candle-light, however, it was astonishingly changed, not having then any blue in it, but being what I called red, a colour which forms a striking contrast to blue. Not then doubting but that the change of colour would be equal to all, I requested some of my friends to observe the phaenomenon; when I was surprised to find they all agreed, that the colour was not materially different from

what it was by day-light, except my brother who saw it in the same light as myself. This observation clearly proved, that my vision was not like that of other persons; and, at the same time, that the difference between day-light and candle-light, on some colours, was indefinitely more perceptible to me than to others. It was nearly two years after that time, when I entered upon an investigation of the subject, having procured the assistance of a friend, who, to his acquaintance with the theory of colours, joins a practical knowledge of their names and constitutions. I shall now proceed to state the facts ascertained under the three following heads:

I. An account of my own vision.
II. An account of others whose vision has been found similar to mine.
III. Observations on the probable cause of our anomalous vision.

I. OF MY OWN VISION

It may be proper to observe, that I am shortsighted. Concave glasses of about five inches focus suit me best. I can see distinctly at a proper distance; and am seldom hurt by too much or too little light; nor yet with long application.

My observations began with the solar spectrum, or coloured image of the sun,

JOHN DALTON

exhibited in a dark room by means of a glass prism. I found that persons in general distinguish six kinds of colour in the solar image; namely, red, orange, yellow, green, blue, and purple. Newton, indeed, divides the purple into indigo and violet; but the difference between him and others is merely nominal. To me it is quite otherwise; I see only two or at most three distinctions. These I should call yellow and blue; or yellow, blue, and purple. My yellow comprehends the red, orange, yellow, and green of others; and my blue and purple coincide with theirs. That part of the image which others call red, appears to me little more than a shade, or defect of light; after that the orange, yellow, and green seem one colour, which descends pretty uniformly from an intense to a rare yellow, making what I should call different shades of yellow. The difference between the green part and the blue part is very striking to my eye: they seem to be strongly contrasted. That between the blue and purple is much less so. The purple appears to be blue, much darkened and condensed. In viewing the flame of a candle by night through the prism, the appearances are pretty much the same, except that the red extremity of the image appears more vidid than that of the solar image.

I now proceed to state the results of my observations on the colours of bodies in general, whether natural or artificial, both by day-light and candle-light. I mostly used ribbands for the artificial colours.

Red (*By day-light*). Under this head I include crimson, scarlet, red, and pink. All crimsons appear to me to consist chiefly of dark blue; but many of them seem to have a strong tinge of dark brown. I have seen specimens of crimson, claret, and mud, which were very nearly alike. Crimson has a grave appearance, being the reverse of every shewy and splendid colour. Woollen yarn dyed crimson or dark blue is the same to me. Pink seems to be composed of nine parts of light blue, and one of red, or some colour which has no other effect than to make the light blue appear dull and faded a little. Pink and light blue therefore compared together, are to be distinguished no otherwise than as a splendid colour from one that has lost a little of its splendour. Besides the pinks, roses, &c. of the gardens, the following British flora appear to me blue; namely, Statice Armeria, Trifolium pratense, Lychnis Flos-cuculi, Lychnis dioica, and many of the Gerania. The colour of a florid complexion appears to me that of a dull, opake, blackish blue, upon a white ground. A solution of sulphate of iron in the tincture of galls (that is, dilute black ink) upon white paper, gives a colour much resembling that of a florid complexion. It has no resemblance of the colour of blood. Red and scarlet form a genus with me totally different from pink. My idea of red I obtain from vermilion, minium, sealing wax, wafers, a soldier's uniform, &c. These seem to have no blue whatever in them. Scarlet has a more splendid appearance than red. Blood appears to me red; but it differs much from the articles mentioned above. It is much more dull, and to me is not unlike that colour called bottle-green. Stockings spotted with blood or with dirt would scarcely be distinguishable.

Red (*By candle-light*). Red and scarlet appear much more vivid than by day. Crimson loses its blue and becomes yellowish red. Pink is by far the most changed; indeed it forms an excellent contrast to what it is by day. No blue now appears; yellow has taken its place. Pink by candle-light seems to be three parts yellow

and one red, or a reddish yellow. The blue, however, is less mixed by day than the yellow by night. Red, and particularly scarlet, is a superb color by candle-light; but by day some reds are the least shewy imaginable; I should call them dark drabs.

Orange and Yellow (*By day-light and candle-light*). I do not find that I differ materially from other persons in regard to these colours. I have sometimes seen persons hesitate whether a thing was white or yellow by candle-light, when to me there was no doubt at all.

Green (*By day-light*). I take my standard idea from grass. This appears to me very little different from red. The face of a laurel-leaf (Prunus Lauro-cerasus) is a good match to a stick of red sealing-wax; and the back of the leaf answers to the lighter red of wafers. Hence it will be immediately concluded, that I see either red or green, or both, different from other people. The fact is, I believe that they both appear different to me from what they do to others. Green and orange have much affinity also. Apple green is the most pleasing kind to me; and any other that has a tinge of yellow appears to advantage. I can distinguish the different vegetable greens one from another as well as most people; and those which are nearly alike or very unlike to others are so to me. A decoction of bohea tea, a solution of liver of sulphur, ale, &c. &c. which others call brown, appear to me green. Green woollen cloth, such as is used to cover tables, appears to me a dull, dark, brownish red colour. A mixture of two parts mud and one red would come near it. It resembles a red soil just turned up by the plough. When this kind of cloth loses its colour, as other people say, and turns yellow, then it appears to me a pleasant green. Very light green paper, silk, &c. is white to me.

Green (*By candle-light*). I agree with others, that it is difficult to distinguish greens from blues by candle-light; but, with me, the greens only are altered and made to approach the blues. It is the real greens only that are altered in my eye; and not such as I confound with them by day-light, as the brown liquids above mentioned, which are not at all tinged with blue by candle-light, but are the same as by day, except that they are paler.

Blue (*By day-light and candle-light*). I apprehend this colour appears very nearly the same to me as to other people, both by day-light and candle-light.

Purple (*By day-light and candle-light*). This seems to me a slight modification of blue. I seldom fail to distinguish purple from blue; but should hardly suspect purple to be a compound of blue and red. The difference between day-light and candle-light is not material.

Miscellaneous Observations. Colours appear to me much the same by moon-light as they do by candle-light. Mr. Boyle observed colours by moon-light to differ from those by day-light.

Colours viewed by lightning appear the same as by day-light; but whether exactly so, I have not ascertained.

Colours viewed through a transparent sky-blue liquid, by candle-light, appear to me as well as to others the same as by day-light.

Most of the colours called drabs appear to me the same by day-light and candle-light.

A light drab woollen cloth seems to me to resemble a light green by day. These

colours are, however, easily distinguished by candle-light, as the latter becomes tinged with blue, which the former does not. I have frequently seen colours of the drab kind, said to be nearly alike, which appeared to me very different.

My idea of brown I obtain from a piece of white paper heated almost to ignition. This colour by day-light seems to have a great affinity to green, as may be imagined from what I have said of greens. Browns seem to me very diversified; some I should call red; dark brown woollen cloth I should call black.

The light of the rising or setting sun has no particular effect; neither has a strong or weak light. Pink appears rather duller, all other circumstances alike, in a cloudy day.

All common combustible substances exhibit colours to me in the same light; namely, tallow, oil, wax, pit-coal.

My vision has always been as it is now.

II. AN ACCOUNT OF OTHERS WHOSE VISION HAS BEEN FOUND SIMILAR TO MINE

It has been already observed that my brother perceived the change in the colour of the geranium such as myself. Since that time having made a great number of observations on colours, by comparing their similarities, &c. by day-light and candle-light, in conjunction with him, I find that we see as nearly alike as any other persons do. He is shorter sighted than myself.

As soon as these facts were ascertained, I conceived the design of laying our case of vision before the public, apprehending it to be a singular one. I remembered, indeed, to have read in the Philosophical Transactions for 1777, an account of Mr. Harris of Maryport in Cumberland, who, it was said, "could not distinguish colours;" but his case appeared to be different from ours. Considering, however, that one anomaly in vision may tend to illustrate another, I reperused the account; when it appeared extremely probable that if his vision had been fully investigated, and a relation of it given in the first person, he would have agreed with me. There were four brothers in the same predicament, one of whom is now living. Having an acquaintance in Maryport, I solicited him to propose a few queries to the survivor, which he readily did (in conjunction with another brother, whose vision has nothing peculiar), and from the answers transmitted to me, I could no longer doubt of the similarity of our cases. To render it still more circumstantial, I sent about twenty specimens of different coloured ribbands, with directions to make observations upon them by day-light and candle-light; the result was exactly conformable to my expectation.

It then appeared to me probable, that a considerable number of individuals might be found whose vision differed from that of the generality, but at the same time agreed with my own. Accordingly I have since taken every opportunity to explain the circumstances amongst my acquaintance, and have found several in the same predicament. Only one or two I have heard of who differ from the generality and from us also. It is remarkable that, out of twenty-five pupils I once had, to whom I explained this subject, two were found to agree with me; and, on another similar occasion, one. Like myself, they could see no material difference betwixt pink and light blue by day, but a striking contrast by candle-light. And, on a fuller investigation, I could not perceive they differed

from me materially in other colours. They, like all the rest of us, were not aware of their actually seeing colours different from other people; but imagined there was great perplexity in the names ascribed to particular colours. I think I have been informed already of nearly twenty persons whose vision is like mine. The family at Maryport consisted of six sons and one daughter; four of the sons were in the predicament in question. Our family consisted of three sons and one daughter who arrived at maturity; of whom two sons are circumstanced as I have described. The others are mostly individuals in families, some of which are numerous. I do not find that the parents or children in any of the instances have been so, unless in one case. Nor have I been able to discover any physical cause whatever for it. Our vision, except as to colours, is as clear and distinct as that of other persons. Only two or three are short sighted. It is remarkable that I have not heard of one female subject to this peculiarity.

From a great variety of observations made with many of the above mentioned persons, it does not appear to me that we differ more from one another than persons in general do. We certainly agree in the principal facts which characterize our vision, and which I have attempted to point out below. It is but justice to observe here, that several of the resemblances and comparisons mentioned in the preceding part of this paper were first suggested to me by one or other of the parties, and found to accord with my own ideas.

Characteristic Facts of Our Vision. (1) In the solar spectrum three colours appear, yellow, blue, and purple. The two former make a contrast; the two latter seem to differ more in degree than in kind.

(2) Pink appears, by day-light, to be sky-blue a little faded; by candle-light it assumes an orange or yellowish appearance, which forms a strong contrast to blue.

(3) Crimson appears a muddy blue by day; and crimson woollen yarn is much the same as dark blue.

(4) Red and Scarlet have a more vivid and flaming appearance by candle-light than by day-light.

(5) There is not much difference in colour between a stick of red sealing wax and grass, by day.

(6) Dark green woollen cloth seems a muddy red, much darker than grass, and of a very different colour.

(7) The colour of a florid complexion is dusky blue.

(8) Coats, gowns, &c. appear to us frequently to be badly matched with linings, when others say they are not. On the other hand, we should match crimsons with claret or mud; pinks with light blues; browns with reds; and drabs with greens.

(9) In all points where we differ from other persons, the difference is much less by candle-light than by day-light.

III. OBSERVATIONS TENDING TO POINT OUT THE CAUSE OF OUR ANOMALOUS VISION

Reflecting upon these facts, I was led to conjecture that one of the humours of my eye must be a transparent, but coloured, medium, so constituted as to absorb red and green rays principally, because I obtain no proper ideas of these

in the solar spectrum; and to transmit blue and other colours more perfectly. Our type of eyes admit blue rays in greater proportion than those of other people; therefore when any kind of light is less abundant in blue, as is the case of candle-light compared to day-light, such eyes serve in some degree to temper that light, so as to reduce it nearly to the common standard. This seems to be the reason why colours appear to me by candle-light, almost as they do to others by day-light.

Comment: Dalton was the very first to record an account of congenital color-blindness. He was a devout Quaker and on one occasion outraged a religious meeting by appearing in a pair of flaming red colored stockings. When he was invested with the scarlet gown of the University, the color seemed to him similar to that of trees. In 1854 Wilson of Edinburgh was led to appreciate the practical importance of color blindness when he discovered that some of his students were unable to judge correctly the colors of chemical precipitates. He made the first suggestion that the color-blind are unfit to become painters, dyers, tailors, chemists, botanists, geologists, physicians, seamen or railroad employees. In the investigation of a serious railway accident in Sweden in 1875 it seemed that color blindness was the probable cause of the disaster. Through the efforts of Holmgren a rule was adopted the following year that only persons with normal color vision were to be employed in the Swedish railroad service; a procedure that has been followed since throughout the world.

BIOGRAPHICAL NOTE

John Dalton (1766–1844) was born in England and spent most of his life as a simple schoolmaster. His only university degree was an honorary LL.D. conferred by the University of Edinburgh when he was 68. At the age of 36 he proposed the atomic hypothesis which was supported by the elaborate experiments of Berzelius eight years later. Before Dalton's interests became dominated by chemistry he had written on English grammar, meteorologic observations, and his own color-blindness. A bust in his honor, which cost $10,000, is placed in the entrance hall of the Manchester Royal Institution, a fitting memorial to one of the world's great scientists.

As a son of a poor weaver, he learned to rely on his own resources from earliest youth. He started teaching at his village school at the age of 12. Every free hour of his life was henceforth devoted to intellectual pursuits. Always financially poor, his crude experiments with crude apparatus eventually led to the discovery of several basic laws of science. His first scientific paper, inspired by his own extreme color-blindness, was the first systematic presentation of congenital color-blindness. He next turned to meteorology and came to the conclusion that the different size of oxygen and nitrogen particles was an important factor in the stable composition of air. This led to the investigation of the number and weight of the chemical elementary principles which enter into any sort of combination, and then in 1808 to the announcement of his atomic theory. Dr. William Prout, an English physician who ardently espoused Dalton's theory, proposed in 1815 the hypothesis that hydrogen was the universal substance, and that the atoms of other elements were really aggregates of hydrogen atoms.

JAMES E. LEBENSOHN

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Reports from Abroad

INDIA

Mathur at the Medical College of Agra has made an entirely new approach to the pathogenesis of glaucoma. He has described, in addition to the usual three spaces, a fourth space termed the "Papillary Space" in front of optic nerve. It is bounded in front by the posterior-limiting membrane and the apex goes far into the lamina cribrosa. The perivascular spaces and the hyaloid canal open into this chamber and drain the retinal fluid backward. He is of the opinion that obstruction to the outflow of this lymph is responsible for the production of glaucoma. If the hyaloid canal is patent, the fluid is pushed into the retro-lental space which, in turn, pushes the lens and iris forward, blocking the angle and precipitating congestive glaucoma (narrow angle glaucoma). If the canal is not patent, the fluid goes on collecting in this chamber, causing optic nerve atrophy and cupping (open angle glaucoma). He has tried to explain the early glaucoma changes, the presbyopic error, the field changes and the optic nerve pathology on this basis. He admits that the dilatation of pupil cannot be explained by this. The concept is certainly thought-provoking although it cannot be regarded as conclusive. At present he is engaged in further elaboration.

Before the concept is accepted it will have to be worked out experimentally that in a number of cases the hyaloid canal is patent and that in an equal number it is closed. The production of glaucoma by forcing the fluid through the central retinal perivascular spaces into the optic nerve head will also have to be shown. The theory fails to explain many facts known about glaucoma. It also fails to explain the absence of glaucoma in cases where the papillary space is obliterated, as in papilloedema and primary optic atrophy. We must, at the same time, await his further observations with interest.

Another approach to the problem from this department is local neuro-vascular approach, essentially based on the neuro-vascular school of Duke-Elder, although differing from it in its being local rather than central in concept. It is believed that there is no difference between simple and congestive glaucoma from the point of pathogenesis and that the classification as two separate entities is unjustified. According to this opinion, glaucoma has two stages—a stage of congestion (which may be clinically evident or not) and a stage of sclerosis. It is quite possible that glaucoma may pass from subclinical stage of congestion to the sclerotic stage without the knowledge of the patient (so-called simple glaucoma).

It has been reported by Agarwal and Saxena and Agarwal and Sharma that in addition to the local pathology (raised tension, increased diurnal rhythm, cup-

ping of the disc, field changes, diminished facility of the outflow and increased local capillary permeability) there are several general changes in glaucoma, e.g., hemodilution, inversion of venous pressure rhythm, increase in general capillary permeability and increase in general capillary fragility. It has also been observed by Agarwal that sympathicolysis does not have lasting beneficial effect in glaucoma. The cases previously reported as cured eventually came back with glaucoma, the only difference being that the congestion became sub-clinical from manifest in them. Agarwal and Saxena have also observed that the formation of aqueous is not permanently decreased after administration of Diamox. Cyclodiathermy also gives temporary response. Agarwal also reported that parasympathetic nervous system does not have any controlling influence on the production of abnormal tension.

It is significant that after local operation of glaucoma, where glaucoma has been cured as seen by arrest in field changes and absence of symptoms and signs, the general changes have also retrogressed. It is also noteworthy that in all these cases facility of outflow is not necessarily increased. It is, therefore, concluded that a disturbance in local axon reflexes produces some toxins which, in turn, are absorbed into the circulation and produce the general changes. The isolation of these toxins and experimental production of glaucoma have not yet been accomplished but is being studied. A simple local operation like trephine or iridencleisis helps to break the vicious circle of axon reflexes which, in turn, probably results in stoppage of production of toxins and regression of local and general disease.

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JAPAN

During the past seven years Dr. Shuzo Ogino of the Department of Ophthalmology of Osaka University Medical School, Nakanoshima, Osaka, has been doing studies on the biochemistry of the lens. Most of the data have been published in Japanese and a summation of the studies was presented at the Japanese Ophthalmologic Society meeting in April, 1955, at Kyoro Medical School. Dr. Ogino kindly agreed to abstract his studies for the Survey of Ophthalmology.

"The lens grows rapidly in the early fetal period and at a relatively constant rate in the adult period. The lens consumes oxygen slightly but definitely. The oxygen uptake of the lens *in vitro* is governed by both enzymatic and nonenzymatic processes.

"The lens decomposes glucose to pyruvate and the serial substances of Embden-Meyerhof's diagram are found in the lens. The process of glucose catabolism in the lens is analogous to that in muscle. Pyruvate is reduced to lactic acid, mainly in the lens cortex while it is oxidized aerobically in the lens epithelium. Pyruvate, α-ketoglutarate and oxalacetate are found in the lens, and these substances are oxidized aerobically by the lens extract. From these facts, it may be assumed that the TCA cycle is present in the crystalline lens. The cytochrome series, riboflavine and co-carboxylase are found in the lens epithelium. Organic phosphate, inorganic phosphate and energy-rich phosphate compounds are found in the lens. The equatorial portion is markedly rich in adenosine triphosphate.

"In the normal lens, ascorbic acid is formed from mannose and glucose but not from fructose, galactose and ribose. These processes are specific to the lens. The phosphate seems indispensable for the synthesis of ascorbic acid. The following biochemical pathway from mannose to ascorbic acid was clarified: Mannose → mannonic acid → diketogulonic acid → dehydroascorbic acid → ascorbic acid. In the cataractous lens, ascorbic acid is oxidized to oxalic acid via diketogulonic acid. Most of ascorbic acid in the aqueous humour seems to have been derived from ascorbic acid already formed in the lens.

"Eighty to ninety per cent of glutathione in the lens is of a reduced form. Oxidized glutathione is converted to reduced form by normal lens extract. This reductase activity decreased by dialysis is reactivated by additional TPN. In the cataractous lens, this reductase activity decreased markedly. The decreased activity is reactivated by additional TPN only in the early morbid stage.

"The cataractogenic agent of naphthalene cataract is β-naphthoquinone. This substance is isolated from the urine of experimental animals as mercapturic acid compounds. The guinea pigs fed on a vitamin C deficient diet developed cataract following injection of benzoquinoneacetic acid. Benzoquinoneacetic acid is excreted in the urine of guinea pigs fed on a vitamin C deficient diet with a simultaneous administration of tyrosine and butyrate, resulting in cataracts. Guinea pigs with scurvy develop black cataract following injection of dopa-quinone. Chickens hatched out of adrenaline-quinone injected eggs developed cataracts. There quinoide cataracts are prevented by vitamin C.

"The animals develop galactose cataract earlier on a hyperprotein diet than on a hypoprotein diet. Guinea pigs fed on a vitamin C deficient diet and administered galactose and tyrosine simultaneously develop cataracts, demonstrating the excretion of benzoquinoneacetic acid in the urine.

"Alloxan diabetic rats develop cataracts very easily on a hyperprotein diet. Benzoquinoneacetic acid is excreted in the urine of alloxan diabetic rat following administration of tyrosine.

"Aminophenol and nitrophenol compounds are largely responsible for the occurrence of cataracts of the guinea pigs fed on a vitamin C deficient diet. Amidol (2-amino-4-aminophenol) is excreted in the urine of rabbit administered dinitrophenol. Guinea pigs fed on a vitamin C deficient diet develop cataract following injection of oxidized amidol.

"Vitamin C deficiency is found in senile patients having cataracts. 5-Hydroxyanthranilic acid, one of the intermediates of tryptophan is isolated from their urine. Guinea pigs fed on a vitamin C deficient diet develop cataracts following injection of quinoneiminecarboxylic acid which is oxidized form of 5-hydroxyanthranilic acid. From these results it is clear that the close relationship between abnormal metabolism of tryptophan and cataract formation.

"Glutathione is synthesized in the lens. Glycine is incorporated to serine in the lens protein. Activities of glutamic acid-alanine and glutamic acid aspartic acid transaminase systems are clearly evidenced in the lens. Considerable phosphatase, adenosine triphosphatase and 1-peptidase activities are demonstrated in the lens. Ascorbic acid and glutathione regulate these enzyme activities.

"β-crystalline acts as a protective colloid for α-crystalline. Cysteine in the lens protein is oxidized to cystine in cataract formation. On the other hand, the soluble protein of lens decreases while the insoluble protein increases. Energy metabolism is closely related with the maintenance of a normal level of water and potassium in the lens."

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Clinical Practice

ACCOMMODATION AND REFRACTION

MYOPIA OF PREMATURITY

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Houston, Texas

Am. J. Ophth. 1955, *40:* 474–481

The development of the eye in 462 premature infants, 136 of whom had retrolental fibroplasia, was studied during the past four years. These infants were found to have a high and fluctuating myopia during the neo-natal period which was more exaggerated in the small infants with immature eyes and in those infants who subsequently developed retrolental fibroplasia. Myopia which was observed early in the course in retrolental fibroplasia may remain as a residual of the disease.

The mechanism for the production of myopia in premature infants appears to be associated with the immature eye. From the embryologic facts and mathematical probabilities there may be an underlying metabolic disturbance in the media of the eye producing changes in axial length, corneal curvature, and index of refraction. Any one or all of these combined could produce a myopia. This process is further altered by retrolental fibroplasia and results in a persistent high myopia. Such abnormalities in metabolism of the media of the developing eye may be conditioned by the infant's abnormal extra-uterine existence.

Comment: In this very interesting paper, the first in which any wide scale attempt has been made to study ocular development in a large number of premature infants, the authors found some correlation between the existence of retrolental fibroplasia and subsequent high myopia. With the lessening incidence of the former disease, because of alterations in the technique of the care of prematures, there will probably be less opportunity in the future to study such relationships. A continued study, however, may shed some light upon the genesis of high and progressive myopia in cases with no history of retrolental disease.

Myopia of high degree seems likely to be a normal condition in a sufficiently premature infant and perhaps can be explained best by considering that for a long period after its complete formation and separation from the surface ectoderm the lens is approximately spherical and thus has a very considerable amount of refractive power, so that even in the short eye of the fetus the optical system would probably be myopic. Not until the subsequent formation of the zonule and the establishment of normal tonus of the ciliary

muscle would the lens be forced to adopt its normal flattened shape, a process which probably may be somewhat incomplete at full term.

Another embryologic consideration is that of corneal development. The small cornea of the fetus, with its short radius and therefore high refractive power, develops very rapidly during the last two months to nearly adult size.

The authors have endeavored to utilize the optics of the reduced eye for a mathematical consideration of their findings. It should be remembered in this connection that the corneal radius in the reduced eye is purely artificial and is designed to give, with a single refracting surface, the same size image as is produced in the schematic eye with its multiple refracting surfaces. The only factor which the reduced eye would have in common with an actual eye is its image distance as measured from the principal nodal point in the reduced eye and the second nodal point in the schematic eye. Calculations which use the corneal radii of the reduced eye are not valid in the consideration of the optical characteristics of the corneal radii of an intact eye, either infantile or adult.

It should also be remembered that an increase in the refractive index of the vitreous humor would not increase myopia, but would tend to decrease it, as it would lessen the relative refractive index between the lens and the vitreous.

The authors should be encouraged to continue this investigation and to, if possible, devise means of obtaining actual measurements of corneal curvature, data which would help greatly in their studies.

EDWIN F. TAIT

CORRECTION OF UNILATERAL APHAKIA WITH CONTACT LENS

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Ophthalmologica 1955, *130:* 329–335

Contact lenses fitted on the aphakic eye give the advantage of fusion and of the use of both eyes together. Additionally, the eye wearing a contact lens has normal appearance and there is no need for the thick, heavy spectacles. The contact lens does not cloud in cold weather, nor does it break; it causes no restriction of the visual field and almost completely restores the normal state.

Aphakic eyes tolerate the contact lens better than eyes wearing them for cosmetic purposes only. A lesion of the corneal nerves during operation may be responsible for this.

Twenty-five patients with monocular aphakia were supplied with contact lenses primarily to restore their binocular vision. Fifteen patients had immediate good binocular vision, four even though heterophoric. Diplopia was present in eight patients and was corrected with a prism. A permanent prism was prescribed in cases of poor fusion where diplopia could not be observed during examination. At re-examinations, which followed within two to ten weeks, patients wearing a prism attained good fusion, diplopia did not even appear without the prism: spontaneous fusion was achieved. Only four patients had to wear a prism later.

Sixteen patients wore the contact lens comfortably without complaints. Four showed a moderate sensitivity and three had definite complaints. Twelve patients wear the lenses regularly, all day, four irregularly and seven only occasionally.

Contact lenses are indicated in monocular aphakia for those whose binocular vision is indispensable for their work and for those patients who want to be fitted. Forced prescription is a mistake.

Comment: Every once in a while in the ophthalmological world some clinician or research worker becomes interested in and often enthusiastic about the use of contact lenses, with or without added ordinary correcting glasses, to provide fusion and single binocular vision in monocular aphakia. That this can be done readily is evidenced by the author of this paper and the experience of many other ophthalmologists who have tried it.

As far as the purely optical considerations are concerned, the refractive error of the aphakic eye may be corrected and the resultant aniseikonia may be neutralized and fusion regained.

Heterophoria or small amounts of heterotropia are not usually a problem if the patient had previously enjoyed good single binocular vision. As a rule, fusion and fusional vergence are reestablished rapidly when the retinal images are properly focused and, if necessary, their sizes adjusted. Unfortunately, however, most patients require conventional glasses in addition to the contact lenses because the unoperated eye usually presents a refractive error and the aphakic eye, with its contact lens, has no accommodative ability, so that an added correction is necessary for focusing at near points. In addition, a component to magnify or minify images must be used if aniseikonia interferes with fusion.

In this country, most ophthalmologists who have had much experience with this problem agree that few of these patients will take the time and trouble to use a contact lens together with conventional glasses, inasmuch as the majority of them learn to adjust quickly to the post-operative situation and develop a monocular or alternating suppression with which they are quite comfortable. In my own experience, about the only ones who persisted with the combined contact lens and spectacle correction were younger and scientifically minded patients who were interested in what they considered a scientific gadget.

EDWIN F. TAIT

THE CORRECTION OF SUBNORMAL VISION— A NEW DEVELOPMENT

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Am. J. Optom. and Arch. Am. Acad. Optom., 1955, *32:* 479–486

The correction of subnormal vision requires magnification of the retinal image to spread the light rays over a wide retinal area or to direct the image onto an unaffected part of the retina. Separate lenses or lens systems for near and for distance may be necessary to achieve this.

The elimination of the various aberrations is difficult and it is impossible to correct them all adequately. Chromatic aberration, including chromatic difference of magnification is due principally to the material of the lens. The form of the lens governs the special aberration, coma, oblique astigmatism, curvature of the field, and distortion. A comprise must be made in the final lens design since some of these aberrations can be most disturbing clinically while others are tolerated.

In distance corrections it is essential that the unit be as compact as possible so that the lenses may be worn permanently. The author's distance lenses are composed of one plastic unit and one completely of glass. The glass system gives a well corrected full field, whereas the plastic unit produces some chromatism and peripheral distortion. The plastic unit, however, is lighter and virtually unbreakable, although susceptible to surface scratches. The central field is smaller but the total field greater than in glass lenses. Where the patient is not disturbed by peripheral aberrations, the plastic unit would appear to be more desirable. Subnormal vision patients find chromatic aberration not troublesome since many have a defect in color perception.

Comment: Ophthalmic lenses made from transparent plastic materials are now being widely used, especially where lightness and safety from breakage are factors. The disadvantages are that perfect refractive surfaces are difficult to obtain and that the lenses are relatively soft and easily scratched.

One other advantage is that the surfaces are produced by molding instead of grinding and this is of great importance in dealing with aspherical curves in which the curve is not a section of a sphere but of a conic section. Grinding aspheric curves on glass lenses is a difficult process. Aspherical surfaces can be designed to avoid peripheral (spherical) aberration in a lens and therefore may be of importance in strongly centered systems such as those in the high power simple magnifiers used in partially seeing cases.

The author of this paper reports his experiences with doublet magnifiers with an aspherical surface on each lens, as well as with glass and plastic doublets with conventional spherical surfaces and with plastic and glass Galilean telescopes. The telescopic and spherical microscopic systems described are essentially those with which workers in the field are already familiar and the results comparable to those reported previously.

Of interest, however, are the comparative figures showing the increase in field of the aspheric microscopic doublet over that possible with a spheric doublet. The former would seem to be the preferred type. However, to one who has worked with aspheric ophthalmic systems, the necessity for keeping the visual axis of the eye continuous with the principal axis of the lens offers a problem. If the lenses are not rigidly centered and the patient looking through their principal axis, the resulting aberration would be worse than that with spherical surfaces. Presumably the patient can be trained in this particular if the wider corrected peripheral field of the aspherical system is considered desirable.

EDWIN F. TAIT

DIFFERENCES IN VISUAL ACUITY MEASUREMENTS OBTAINED WITH DIFFERENT TYPES OF TARGETS

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Psychological Monographs 1955, *69:* No. 10, 1–12

An experiment was conducted using 32 subjects to compare visual acuity measurements obtained with different types of commonly used visual acuity targets. The targets consisted of Snellen letters, the Landolt circle, the tumbling (illiterate) "E," the Ortho-Rater checker-board and the Telebinocular Dot-test object. Variables such as distance and lighting were held constant.

Results of a statistical analysis showed that visual acuity measurements differed significantly as a function of target, but not as a function of the interaction of fatigue and practice or of the order of presentation. Retinal resolution and brightness discrimination determined performance on the various tests. The relative area of block present in critical elements of targets of the same size was found to be correlated positively with the fineness of threshold.

Generally a test composed of Snellen letters differs in difficulty from a dot-type positional test or from the tumbling (illiterate) "E" test. Since these thresholds are not likely to be equivalent in individual cases, extreme caution is urged in the substitution of the scores of one such test for the scores on another. Thus, a visual acuity of 20/20 on the tumbling "E", on the Snellen letter chart, and the dot-type test means, in each case, a different level of visual acuity.

The meaningfulness of Snellen letter thresholds is limited by the finding that letter difficulty is a function of what letters are combined in the test. Separation of Snellen letters into homogenous groupings on the basis of legibility changed the relative difficulty of those groups. The "easiest" and the "most difficult" groups were significantly less difficult than the "intermediate" group.

Comment: Experimental workers have shown repeatedly that shape, size, and relations of other portions of a target will affect an acuity determination, where acuity is measured by the visual angle subtended by a "critical element" of the target. The immediate practical significance of this fact is that results on one target should not be directly compared with results on another, unless the correction factor is known. Snellen letter targets demand less resolution of critical elements than is required of certain other targets, perhaps because of cues from outline contours of letters. Some letters are obviously more easily discriminated than others, so there is the additional problem of making one set of letters comparable to another.

The study made by Rabideau of his data by a factor analytic method suggests that even the use of correction factors might be misleading. Two different targets may be measuring two or more kinds of acuity. When such distinctions might become important must be determined by further work. Isolation of retinal resolution from brightness discrimination as two factors which are usually confounded in determinations of acuity might prove to have both clinical implications and significance for personnel practices.

Psychophysiologists have tended to work with even simpler targets than these used typically in the clinic. Such problems as the effect of adjacent contours on resolution of test contours, and the specification of conditions under which increasing illumination increases, fails to increase, or even decreases acuity are of interest in the pursuit of fundamental knowledge about visual processes.

AUSTIN RIESEN

THE GLOBE

OCULAR PROSTHETICS

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A.M.A. Arch. Ophth. 1955, *54:* 733–742

Plastic artificial eyes may be classified as follows: 1. The Snellen conventional re-form eye which has a horizontal dimension approximately 10 per cent greater than the vertical dimension. 2. The conventional shell type, similar to the re-form eye but constructed so that the scleral portion is about 1 to 1.5 mm thick. This type is indicated when a prosthesis is fitted over a phthisical eye or protruding buried implant. 3. The cosmetic contact shell is worn like a scleral contact lens and is indicated for the cosmetic correction of a disfigured eye. 4. The corrected contact cosmetic shell which is similar to three, but contains an optical correction in the pupillary area. It is indicated in albinism, aniridia, photophobia and the like. 5. Semishell eyes are composed of one-half a conventional re-form and the other half a shell, which are used when one fornix is normal and the other shallow. 6. The shelf type is a conventional re-form eye with a shelf at the top and is indicated in cases of poor socket and shallow lower lid. 7. The curl-back shell has a shelf above and below and is indicated in cases of shallow or deficient inferior fornices. 8. The forty-five-degree-bend re-form eye has the upper temporal portion bent backward and is worn when the ordinary re-form would lean back. 9. The peanut eye is a conventional re-form with the horizontal portion elongated and the vertical shortened. 10. The reverse shape is a re-form eye with the vertical dimension greater temporally so that it will not rotate in the socket. 11. The front build-up is a re-form eye built up at the upper scleral periphery to prevent drooping of the lid.

The Mules sphere is preferred for implant, usually 18 mm. in diameter to replace a globe 24 mm. in diameter. To obtain the best functional and cosmetic results the enucleation should be done with a minimum of trauma and the greatest possible tissue preservation.

The following method is recommended for examining prosthetic eyes:

1. The eye is examined grossly and compared with the normal eye. A check is made for any obvious deformities, such as the eye falling too deep into the socket, giving an appearance of enophthalmos. The prosthesis should be secure, should match the other eye in color and width of the palpebral fissures, and should approximate that of the normal. The lids should close firmly and easily, and the lacrimal puncta should fall against the globe. There should be no eversion of the lower lid or falling in of the superior palpebral sulcus.

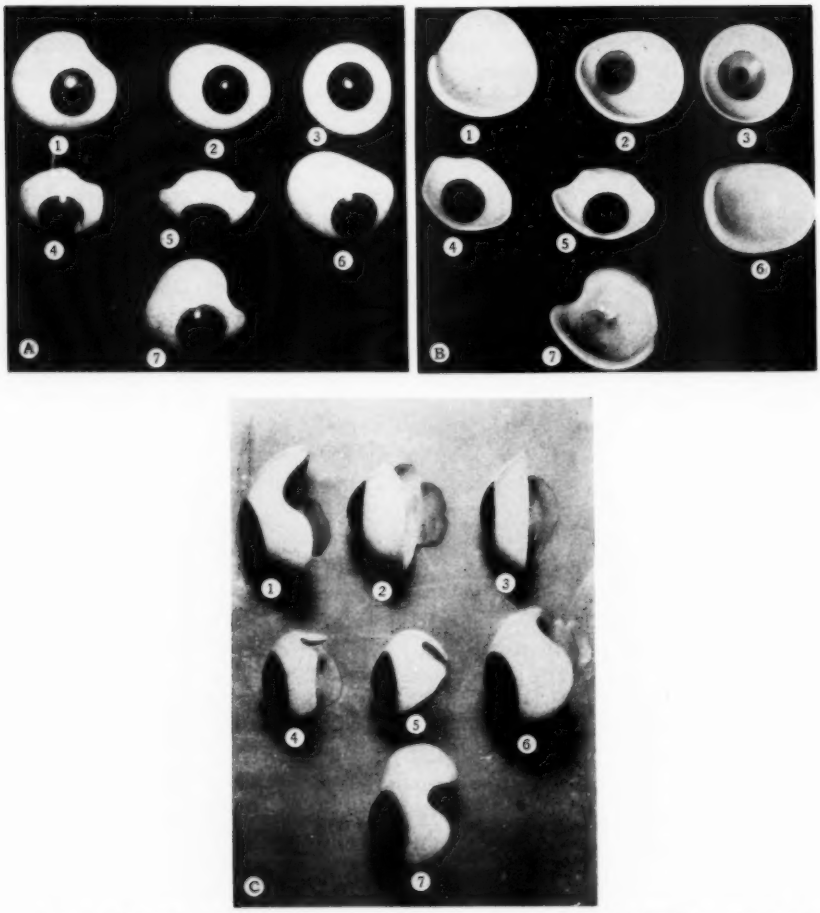

FIG. 1. (Zekman, Ladenheim and Scott.) Types of prosthesis: (1) Snellen reform eye; (2) Shell eye; (3) Cosmetic contact shell; (4) Shelf type; (5) Curl-back type; (6) Peanut re-form type; (7) Superior build-up. A: Anterior view; B: Posterior view; C: Side view. (Reproduced with permission, A. M. A. Arch. Ophth.)

2. With a pocket flashlight, the corneal reflex is checked. A bright reflex indicates a well-polished prosthesis, whereas a dull reflex indicates erosion and collections of deposits, the source of possible irritation to the palpebral conjunctiva.

3. The corneal reflex is checked for esotropia, or hypertropia with the eye in the primary position.

4. Motility is checked in the cardinal positions of gaze. It is obvious that it will be a rare prosthesis that will match a normal eye for movement.

5. Removal of the prosthesis is a problem only when a glass prosthesis has been

used, in which case it is far more prudent to let the patient remove the eye. Plastic eyes obviate the problem of breakage.

In removing the prosthesis, the object is to permit air to enter between the prosthesis and the conjunctiva, so that the negative pressure is neutralized and the appliance may be easily removed. This is best done by pulling the lower lid down and having the patient look up. A rubber suction cup may be used.

6. The socket is examined for any signs of inflammation, scarring, secretions, or pockets of retained secretions.

7. A comparison is made of the shape of the prosthesis and the shape of the socket. The periphery of a proper-fitting prosthesis should follow the basic contour of the cul-de-sac of the socket.

8. The prosthesis is examined. A dull finish or knife edges or rough edges on a plastic eye or pitting on glass eyes will indicate mineral deposits on the surface. These deposits are a constant source of irritation, causing inflammation.

9. The patient is queried as to the length of time he wears the prosthesis before removing and cleaning it. Some physicians recommend weekly or biweekly instillations of 1:5000 solution of benzalkonium (Zephiran) chloride drops, whereas others prefer the use of antibiotic drops or ointments. It has been reported that the routine use of benzalkonium chloride causes the formation of proteinaceous deposits, which may cause irritation, discomfort, and excessive secretion.

Wearing the prosthesis for too long a period may in itself cause pitting of glass eyes and irritation. It is preferable to specify that the appliance be cleansed with soap and water at precise intervals, of one to six weeks, the frequency always depending on the individual case. Liquid petrolatum or methylcellulose alleviates discomfort and is sometimes advised.

Comment: This article expresses the opinions of most ophthalmologists, including this editor, in regard to the comparative advantages of the oldest and simplest implant, the Mule's sphere, compared to the various types of integrated implants. It is now common experience that the best results are obtained using a completely buried implant and the services of an expert prosthetist, who can make special artificial eyes, to fit individual sockets. Motility of such special prostheses may not be equal to that when integrated implants are employed in the immediate post-operative period, but none of the unpleasant complications of integrated implants such as excessive discharge or an extremely high extrusion rate, follow the use of completely buried implants. Pictures of some of the authors' end results would suggest that even with the simpler and more conservative techniques, excellent cosmetic effects may be achieved.

DANIEL SNYDACKER

THE LENS

THE KERATOME SCISSORS INCISION IN CATARACT EXTRACTION: THE ADVANTAGES AND DISADVANTAGES

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Trans. Ophth. Soc. S. Africa, 1954, 1–10

Experience obtained in a series of 400 cataract operations performed during the period from 1946 to 1954, in which the keratome-scissors incision was used routinely, reinforces the belief that this incision possesses many advantages, over one made with a Graefe knife, especially for the average surgeon, who is not gifted with great dexterity. A bad incision is never made when the keratome is used, because (1) the surgeon always uses the right hand in making the incision; (2) he is more relaxed; (3) the patient is less apprehensive; and (4) the conjunctival flap can be cut to the desired width and the surgeon is always assured of a good flap, covering the whole incision. After the flap has been cut, the conjunctiva is stroked back over the cornea and the limbus is cleared of conjunctiva with a few strokes of a corneal splitter. A little extra time may well be spent on this procedure, because it makes it certain, that the incision will be placed in clear limbal tissue and not in the sclera. All bleeding points are then touched with the hand cautery, which gives the surgeon a bloodless field and eliminates annoying bleeding into the anterior chamber which so often complicates the Graefe incision. Three "anacap" conjunctival scleral stitches are then inserted, picking up the scleral tissue about 2 mm. from the limbus, and are turned back over the towel covering the brow, to be used later after the incision has been completed. For the keratome, the author prefers a fixation spot above in the 2 o'clock meridian, about 4 mm. from the limbus, where a good grip can be obtained on the episcleral tissue. A slight upward and forward lift should be exerted as the keratome is introduced. When this method of fixation is used, there is very little danger of pressure on the globe. The point of the keratome is then engaged in the limbal tissue at 11 o'clock and pushed through until practically the whole width of the keratome is engaged in the wound. To avoid injury to the lens capsule, attention is given to the point of the keratome as it passes through the anterior chamber, to keep it from being angled too far backwards. Such injury is of no consequence in an extracapsular extraction, but is annoying when an intracapsular extraction is intended. The incision can now be enlarged with the corneal scissors as required. With a little care, there is very little danger of injury to the iris. When the scissors are properly sharp, the cuts will be as clean as those made with a knife, and healing, which may be delayed in wounds with ragged edges, will take place promptly. Before proceeding with the delivery of the lens, the conjunctival flap should be stroked back into place and the two outer stitches

completed. The central stitch is left to be closed after the lens has been delivered. The closure obtained by this method is so firm that a corneal suture is not considered necessary.

Postoperatively, the advantages of the keratome-scissors incision are (1) more rapid re-formation of the anterior chamber and closure of the wound; (2) less tendency to prolapse of the iris; (3) reduced incidence of hyphaemia; and (4) less postoperative astigmatism.

By contrast with its many advantages, the disadvantages of the procedure, which lie in the fact that it takes a little longer to perform; that the keratome enters the anterior chamber blindly for the first 2 mm.; that the incision must be enlarged with the scissors; and that congestion of the conjunctiva persists a little longer, are slight.

Comment: The use of a keratome scissors or a Graefe section in cataract surgery will naturally depend on the preference of the surgeon. There is no question that a keratome scissors section is sometimes more ragged than a Graefe section. Just how that delays healing has not been determined. The Graefe section is quicker and cleaner, but more difficult for some surgeons and difficult for all in those patients who have a shallow anterior chamber.

The use of corneal scleral sutures is to be preferred over scleral conjunctival sutures.

P. Robb McDonald

CORNEAL SUTURES AND LATE EMPTYING OF ANTERIOR CHAMBER

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Arch. chil. de oftal., 1955, *12:* 75–81

Late emptying of the anterior chamber is one of the most frequent complications of cataract surgery. It occurred in 12 per cent of the 418 patients undergoing operations for cataract. In five per cent of these cases aphakic glaucoma followed. Emptying of the anterior chamber occurs, as a rule, on the 10th or 12th day after the operation when the patients have already been discharged from the hospital or are about to be discharged in excellent condition. In a few cases the chamber reforms spontaneously some hours later but, in most cases, 10 or 12 days must elapse before the chamber is reestablished. Complications may or may not occur.

Various theories have been suggested to account for this enigmatic complication. They include: postoperative detachment of the choroid, leakage of aqueous humor through the operative wound, expulsion of aqueous humor produced by

internal vitreous hernia (through the pupil into the anterior chamber) without leakage of the operative wound, and faulty healing of the wound.

Clinical observations led the author to believe that corneoscleral sutures which are left in place for several days after the operation incite necrosis around the suture and microfistulization of the cornea with consequent emptying of the chamber. The following facts supported this theory: Superficially placed corneoscleral sutures frequently fall out spontaneously and, in these cases, flattening of the anterior chamber does not occur. On the other hand, deeply placed corneoscleral sutures when observed in cases of late emptying of the anterior chamber are found to be still in place and have to be cut to be removed. The small zones of necrosis around the sutures are perfectly visible on macroscopic examination of the eye on which the cataract operation was performed.

To prove the truth of this theory, experiments were performed on rabbits, in the eyes of which corneoscleral sutures, such as those used for suturing cataract incisions, were inserted. A limbal incision, 3 mm. long, including half the thickness of the cornea was made. McLean corneoscleral sutures were made with Kalt's silk (6–0). The animals were sacrificed at varying intervals and the eyes were sectioned for microscopic study, particular attention being paid to the zones around the suture at periods ranging from 2 to 12 days after the placing of the suture. After three days a heavy polymorphonuclear infiltration of the cornea in the vicinity of the sutures was observed. The reaction progressed into necrosis, after seven days. There was complete healing in 12 days.

Independent of the author's experiments, and during their course, a report was made by other researchers dealing with experiments in the same field, carried out on monkeys. Comparison of the results of both experiments shows that the tissue response of the cornea to suture is more rapid in rabbits than in monkeys.

Deeply placed sutures tied extremely tight may cause secondary deformation of the pupil, generally seven or eight days after the operation. In these cases, the anterior half of the incision is closed with overriding of the borders, whereas the posterior half of the incision remains slightly open. Fistulization of the suture provokes insignificant leakage of aqueous humor with consequent prolapse of the iris to the open posterior half of the incision and formation of a cystic scar. On the other hand, extremely superficially placed sutures loosely tied may be the cause of faulty healing, frequently complicated by hyphema. In this case, the fibrovascular plug of episcleral tissues in the vicinity of the suture covers the anterior portion of the wound, and starts forming many fibroblasts. Then it bridges the open portion of the wound and during this bridging the plug of episcleral tissues may rupture with subsequent hyphema.

Corneoscleral sutures should be neither too deep nor too superficial and they should not be tied either too tightly or too loosely. In placing corneoscleral sutures, only one-third or one-half of the thickness of the corneal tissue should be taken with the needle in every bite, that is, the needle should be introduced at a point not farther than a third or a half the thickness of the cornea and pulled out as near as possible to the edge of the incision. The silk or thread should be tied firmly, but without any tension. The most convenient number of sutures is three. An excess number of sutures delays healing.

Comment: The use of corneal scleral sutures in cataract surgery has undoubtedly reduced the complication of iris prolapse, delayed formation of the chamber, and has also permitted early ambulation.

Though a change in technique may reduce certain complications, it may also cause unsuspected complications. Corneal sutures that are too deeply placed, or too tightly tied, may produce a complication one is trying to avoid, i.e., a shallow anterior chamber. Evidence of localized edema about one of the sutures in the presence of a shallow chamber, is an indication to remove the suture.

P. Robb McDonald

DEVELOPMENTAL CATARACT

Edme Regnier

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Arch. Pediat., 1955, *72:* 141–146

Cataracts in babies, whether present at birth or formed during infancy, should be termed developmental rather than congenital, because the development of the lens in the human eye proceeds steadily without any particular change in progress at the time of birth. Such cataracts, which occur in every degree of severity from a slight opacity in only one eye to total opacity in both eyes, are seldom discovered before the infant is several weeks or months old. Fortunately, serious, vision-impairing cataracts occur in fewer than 1 in 100 children. Many children with developmental cataracts, however, will have other associated eye defects, and some will also have non-ocular congenital abnormalities.

Examination should begin with an attempt to determine the child's visual acuity, which has an important bearing on the prognosis. Some information may be obtained from his ability to fix a light, from the presence or absence of nystagmus and from the density and location of the opacities in the lens. If possible, the corneal microscope and slip lamp should be used. Knowledge of the lens structure and its zones of discontinuity may indicate the type of cataract and help to determine whether it will be progressive.

Inadequacy of vision is the major indication for surgical treatment, with an unpleasantly white pupil or a greatly constricted visual field ranking next. A visual acuity below 20/70 is not adequate for school work and if the vision is less than 20/200, even central fixation will not be possible. The goal to be attained is an adequate pupil and avoidance of complications; if these are reached the operation may be considered successful even though the resultant vision is still poor because of associated defects. The choice of operation usually lies between needling, discission, and linear extraction, all of which sometimes produce favorable results but none of which can be recommended to the exclusion of the others. Statistical analyses show that final vision is better if the operation is per-

formed after the age of two and one-half years, but earlier intervention may be required in children without adequate vision in either eye. If "good vision" is set at 20/70 or better, 60 per cent of the eyes treated will reach that level if no other ocular defect is present; when other defects are present, however, the rate will be only 10 per cent. Thus the factor most determinative of the result is one over which neither the pediatrician nor the eye surgeon has any control whatever.

Comment: We join the author in the plea, for a more widespread acceptance of the concept, that cataracts, in babies, are developmental rather than congenital. Congenital implies only a point in time and should have no other meaning. The point, made by the author, that many associated ocular abnormalities may co-exist and should be meticulously searched for may be profitably expanded to include a careful physical and biochemical study of these afflicted infants. Our experience has revealed a rather high incidence of associated constitutional and developmental diseases and these children are frequently "poor protoplasm."

We agree that surgical interference, preferably needling followed by linear extraction, should be postponed until the child is beyond two and one-half years of age whenever possible, the incidence of complications dropping *pari passu* with the increasing development of the eye. An optimistic prognosis in developmental cataract surgery should never be made. Vertical nystagmus, in general, can be anticipated to indicate a better final visual acuity than horizontal nystagmus. Information concerning the experience and final visual results secured in the treatment of siblings or parents will make the advise in regard to prognosis more accurate. A visual acuity of 20/70 may suffice, in certain children, to carry them well into the first or second grades, at which time a better appraisal may determine if surgical interference is necessary. A trial of school, thus, is urged.

HAROLD F. FALLS

INTRAOCULAR IMPLANTATION OF ACRYLIC LENS: RIDLEY'S OPERATION. RESULTS

C. ESPILDORA LUQUE, A. GORMAZ, G. LAMA S. M. AND A. VILLASECA

Ophthalmic Clinic Hospital of Salvador

Arch. chil. de oftal., 1955, *12:* 56–59

Intraocular implantation of an acrylic lens was performed in 10 cases of senile traumatic unilateral mature cataract. The authors closely followed Ridley's original technique of extracapsular extraction. In all cases an ample anterior capsulectomy and an abundant careful lavage of the anterior chamber and of the capsular sac were made. After completion of the lavage, the acrylic lens was implanted, and this procedure proved to be less difficult than had been feared. The acrylic lens was slipped into position through the lower border of the pupil,

which was dilated to a diameter of 6 mm. if possible. The lens can, however, be slipped into place behind a pupil of a smaller diameter, provided that the pupillary sphincter and the iris are not rigid. After the operation, the pupil was kept in moderate mydriasis in order to prevent its occlusion as a result of postoperative iritis, in case the latter developed. Cortisone proved to be very efficacious in preventing postoperative iritis. Postoperative posterior adhesions may develop. They do not interfere with the degree of vision obtained as final result of the operation unless they are associated with organized films on the anterior face of the lens or with opacification of the posterior capsule. Vitreous loss did not occur during introduction of the acrylic lens in any of the cases. Early or late increase in the intraocular pressure was not observed. Ridley's original acrylic lens, composed of Transpex and placed in good position, is well tolerated by the eye. Transient mild irido-cyclitis occurred in some cases just as it may occur after operations performed by the common extracapsular methods. In evaluating the results, the patients are considered in three groups of six, two, and two patients, respectively. The results were good in patients in the first group, doubtful in those in the second group, and poor in those in the third group. Vision was over 5/30, without glasses, in all six patients in the first group. In five cases vision did not diminish during the follow-up period of two years after the operation, but was on the contrary maintained and improved. In a patient, 72 years old, vision diminished from 5/50 one month after the operation to 1/30 four months after the operation. This diminution of vision was due to plastic irido-cyclitis which complicated lowering of the patient's general condition after a serious illness. After the illness, a cataract in the other eye was removed by intracapsular method, and 10 days later plastic irido-cyclitis appeared. Vision in this eye is limited to shadows. The useful eye—the one on which Ridley's operation was performed—has a permanent vision of 1/30 (non-modifiable by glasses). Vision in the two patients in the second group was 1/40 and 1/20 34 and 21 days after the operation, respectively. These patients could not be followed any longer. However, when they were observed for the last time on the 34th and 21st days after the operation, the condition of the eyes was promising. It is hoped that vision in the eyes of these patients increased 40 or 60 days after the operation. In the last group (two patients) the results were definitely poor. The operation was complicated by an acute inflammatory reaction of the iris without any other complications. One of the patients had a good tolerance to a second operation performed for the purpose of cleaning the anterior face of the acrylic lens. The vision increased slightly after the second operation. Although the number of cases reported is small, the authors consider Ridley's operation highly promising. It is harmless, well tolerated, and very effective. It solves the problems of the treatment of unilateral aphakia and will, in the future, probably solve that of bilateral aphakia also. The patients are free from the countless inconveniences of the use of biconvex glasses. In cases in which implantation fails, the acrylic lens can be removed without any danger to the patient's eye and the aphakia can then be corrected by the use of adequate glasses.

RIDLEY LENS IMPLANT: CASE REPORT

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J. Louisiana M. Soc., 1955, *107:* 374–376

The Ridley lens implantation operation, in which an acrylic plastic lens is substituted for the cataractous lens, offers a way to achieve binocular vision. If successful, it would do away with the need for heavy lenses and the decrease in the field of useful vision that now follow cataract extraction. Permission was therefore obtained to give it a trial in a carefully selected 75-year-old woman whose vision had been gradually decreasing during the previous two years. Vision was light projection in the right eye, and 20/100 in the left eye. A completely mature cataract was present in the right eye. The vision in the left eye decreased to 20/200 and operation on the right eye was advised. A standard extracapsular linear extraction was performed and as much of the anterior portion of the capsule as possible was removed. The anterior chamber was irrigated and the acrylic lens was introduced by forceps and teased into position with an iris repositor.

When the sutures were removed there was evidence of an iritis and pigment and cellular deposits on the acrylic lens was noted. The cornea was clear and only mild flare was present. The best vision obtained four months following surgery was 20/50 with a −4.00 D. cylinder. Seven months post-operative the eye was quiet, although pigment deposits remained on the lens and a few keratitic precipitates were present on the corneal epithelium. With a +1.00 Sph.−3.50 Cyl. Ax. 110, vision was 20/30.

Although the patient is happy with the present visual acuity and has never complained of distortion or magnification of objects, the operation is obviously not the safest procedure in cataract surgery. Some reaction, of course, was to be expected with this type of extracapsular extraction in a patient of her age, but the reaction she experienced was a combined one due both to the lens material and the foreign body. The unusual amount and axis of the astigmatism may have been due, in part, to a tilting of the plastic lens, although it appeared to be perfectly placed by microscopic examination.

Subluxation of the lens has not been mentioned as a possible complication, but it may conceivably occur. One writer, fearing this possibility, has devised a stainless steel wire attachment to be left embedded in the corneal-scleral wound. Present indications are that until a more innocuous plastic material has been produced and a more accurate method of placing the lens worked out, the Ridley operation should be reserved for patients who must undertake a great risk to gain a very small advantage.

Comment: The use of the Ridley implant is still a very controversial subject. Unquestionably, there are many patients who obtain a very satisfactory result, but when complications do occur, they seem to be more serious than those occurring in the usual cataract procedure.

There are a few patients in this country who are now returning to have their second eye operated on by this technique. They are quite happy about the result, and are firmly convinced after talking to their friends, that the new method is better than the old. The introduction of a foreign body into the eye is to this reviewer an unsound procedure, and, despite the difficulties of an aphakic lens, the conventional operation would seem to be safer.

P. Robb McDonald

THE CORNEA

EFFECT OF SURFACE ANESTHETICS ON THE REGENERATION OF CORNEAL EPITHELIUM

H. J. Küchle

Klin. Monatsbl. f. Augenh. 1955, *126:* 313–320

A comparative experimental study was made of four surface anesthetics, namely, cocaine hydrochloride, tetracaine hydrochloride (Pontocaine), synthetic cocaine tartrate (Psicaine) and p-propyl-amino benzoic acid-γ-dimethylamino-β-oxypropyl ester hydrochloride (Cornecain) to determine their effect on the regeneration of the corneal epithelium of rabbits. The results obtained showed that all four local anesthetics definitely delay the regeneration of the corneal epithelium. Epithelization of defects which were produced in the cornea of the rabbit by vapor cautery, was impaired considerably by Pontocain, somewhat less by Psicaine and Cornecain, and least by cocaine.

From these experimental results practical clinical conclusions may be drawn. When local anesthetics are employed in the presence of corneal lesions, one must keep in mind that such substances, particularly in higher concentrations and with repeated application, may exert an unfavorable influence on the normal course of regeneration and may, thus, enhance the liklihood of secondary infection. For this reason the use of local anesthetics should be limited as much as possible; they should never be applied by the patient himself without control, and one should be cautious in the selection of higher concentrations when, it might be possible to achieve the same effect with a lower concentration. The experimental observation that cocaine caused the least delay in regeneration and only insignificant impairment of the cornea is in contrast to the clinical experience that of all anesthetics, cocaine especially may produce temporary alterations. This apparent variance may be explained by the fact, that the cornea of herbivores is less sensitive to cocaine than the cornea of carnivores.

Comment: It has been known for many years (the work of Liebman and Gunderson, Hermann and Marr, Friedenwald, and Smelser) that local anesthetics will interfere with epithelial regeneration. Küchle's studies would tend to confirm this inhibitory property of local anesthetics. Küchle did not find cocaine to be as harmful in this respect as Pontocaine or Cornacain. Studies such as this stress the necessity for not abusing the use of local anesthetics for ocular diseases. They must be used sparingly and their interference with wound healing kept to a minimum.

Irving H. Leopold

STATISTICAL CONSIDERATIONS ON 426 CASES OF HERPES CORNEAE TREATED AT THE OPHTHALMOLOGIC CLINIC OF BASEL

AUGUST PETERHANS

Ophthalmologica 1955, *130:* 244–271

Of 145,208 patients who were treated between 1939 and 1949 at the ophthalmologic clinic of Basel, Switzerland, a diagnosis of herpetic inflammation of the cornea was made in 426 patients, of whom 124 were women and 302 were men. Thus, one case of herpes of the cornea occurred in approximately 300 cases of eye disease, including non-inflammatory eye conditions. In the women patients the right eye was affected in 67, the left eye in 51; both eyes were affected in six. In the men the right eye was affected in 147 cases, the left eye in 136 cases; both eyes were affected in 19 cases. The incidence of herpes of the cornea, therefore, was approximately the same in both eyes and in both sexes. Using Marchesani's neurosegmental classification of the eye, the five sectors of the cornea, were studied with regard to the location of the herpes. The center of the cornea and the lower corneal sector were more frequently affected by herpes than the upper sectors. In 84 patients herpes of the cornea occurred as secondary disease, and in 40 of the 84 patients it developed after influenza. The incidence of herpes of the cornea, however, was insignificant in relation to the total number of 44,169 cases of influenza which were reported in Basel between 1939 and 1949; there does not seem to be any relationship between the herpes and the influenza virus. The herpetic inflammation of the cornea was ushered in by trauma in 85 of the 426 patients, i.e. a ratio of 20%. Injuries of the cornea without herpes as sequela occurred in 8346 patients. It seems, therefore, likely that herpes of the cornea occurs after trauma of the cornea in only one per cent of the cases. Recurrence of the herpetic inflammation of the cornea occurred in 27 of the 124 women and in 71 of the 302 men. The number of recurrences varied from one to nine; the incidence of recurrences was higher in men than in women. Careful prophylaxis against colds and trauma may reduce this number. The period of healing did not depend on the occurrence of trauma, or the age of the patient. The interval between the onset of the disease and the beginning of treatment had an influence on the period of healing, since delayed treatment was associated with a prolonged course of the disease. In only 44 (10.3%) of the 426 patients did complete healing occur without scar formation.

Of the 426 patients, 352 had superficial herpes, while in 59 patients keratitis disciformis developed, and 15 patients were lost to follow-up. As regard the period of healing, it appeared that superficial herpes of the cornea might be as refractory as keratitis disciformis. The final vision seems to be partially determined at the onset of the disease. The aim of treatment should be to shorten the period of healing. Of the 426 patients 245 had their lesions cauterized by iodine; 52 had iodine

cautery combined with abrasion, four had abrasion only, and 125 had neither iodine cautery nor abrasion. Of the 245 patients treated with iodine alone, 120 patients (49%) had a final vision of more than 6/12, 96 patients (39.2%) had a final vision of 6/15 to 6/30, and 29 patients (11.4%) had a final vision of less than 6/30. Of the 52 patients treated with iodine and abrasion, 28 patients (54.1%) had a final vision of more than 6/12, 17 patients (32.6%) has a final vision of 6/15 to 6/30, and seven patients (13.5%) had a final vision of less than 6/30. Of the 125 patients who were not treated by iodine cautery or abrasion, 52 patients (41.6%) had a final vision of more than 6/12, 42 patients (33.6%) had a final vision of 6/15 to 6/30, and 31 patients (24.8%) had a final vision below 6/30. It seems that iodine cautery may reduce to a certain extent the risk of decreased vision. There is no stereotype treatment for herpetic inflammation of the cornea, but the author strongly cautions against the use of the keratome for abrasion; cotton applicators moinstened with iodine should be used.

Comment: James F. Allen of Tulane University, among others, has pointed out the dangers of too vigorous cautery of the cornea with iodine. It is his opinion, that in many patients with dendritic keratitis the persistent inflammation of the cornea is actually an iodine burn rather than a continuation of the herpes simplex infection. To avoid the dangers of too vigorous cautery he recommends that the initial treatment consist of iodides administered orally and that cautery be postponed until the effect of at least five days of this therapy is observed. The initial cautery with iodine should be very gentle, using a small wisp of cotton as applicator and destroying the epithelium only in the region of the lesion.

Nearly all are becoming familiar with the complications of steroid therapy in herpes simplex, Much of the danger arises from the deceptive improvement which occurs in these eyes when cortisone or its newer derivatives are applied locally. The eye becomes white, the patient no longer complains of photophobia or irritation and the lesion is inconspicuous. The cornea in the area of involvement, however, seems to slowly melt away and an excavation progressively deepens. This area ultimately perforates—an unheard of complication prior to the steroids.

THE OCULAR MUSCLES

SUBNORMAL BINOCULAR VISION WITH SPECIAL REFERENCE TO PERIPHERAL FUSION

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Brith. J. Ophth. 1955, *39:* 474–487

There are many cases of squint in which, in spite of adequate surgical and orthoptic treatment producing equal vision in each eye and restoring approximate parallelism of the visual axes, binocular single vision has not been restored. In many of these cases a fairly strong "binocular union" appears to have developed so that the patient apparently employs his two eyes together with obvious benefit to his visual judgment. Yet examination on the major amblyoscope may show gross central suppression, sometimes absence of fusion, and invariably defective stereopsis. A likely explanation is that a "binocular union" is brought about by a fusion mechanism which links the visual fields of the two eyes in the area of "field overlap".

A review of two hundred consecutive cases of non-paralytic convergent strabismus treated at the authors' hospital during 1950 to 1952 showed that they could be divided into three well-defined groups:

(1) Functionally satisfactory (patients in whom binocular single vision had been fully restored..... 39 (20 per cent)

(2) Cosmetically satisfactory

(a) Subnormal binocular vision (equal or nearly equal acuity, normal retinal correspondence amd doubtful fusion..... 88 (44 per cent)

(b) Grossly defective binocular vision (intractable amblyopia, abnormal and lack of normal retinal correspondence..... 73 (36 per cent)

An analysis was made of the state of binocular vision of 200 consecutive and unselected patients with convergent squint treated during the period 1950 to 1954 by operation and/or orthoptic treatment and occlusion. The patients were divided into groups as shown above.

To discover whether visual judgment was better in patients with subnormal binocular vision (Group 2b) than those with a gross defect of binocular vision (Group 2c) twenty patients from each group were examined on the Livingston rotating depth perception apparatus. All of the patients in the two groups had a poor performance compared to the normal controls who had binocular single vision. If anything the performance of those with subnormal binocular vision was slightly worse than those with grossly defective binocular vision.

The existence of peripheral fusion may enable a patient to maintain parallelism of the visual axes in spite of a central suppression and may account for the infrequency of consecutive divergence in certain cases of squint. This possibility

was investigated in twenty patients with defective binocular vision, by means of the screen test, and in thirty by means of the stereoscopic test. The results were varied and inconclusive owing to the subjective nature of the tests but peripheral fusion with a varying degree of peripheral suppression could be demonstrated in all cases in which normal retinal correspondence was present.

Comment: The visual act of the squinter offers no end of fascinating problems. Their complexity becomes more apparent the deeper one delves into them. One of the most intriguing problems is posed by the question: what keeps the eyes of some people aligned despite the absence of normal binocular vision? There are a number of possible answers to this question. One of them is that the cooperation of periphery of the two retinas, not tested by the usual methods, may supply the necessary control of the position of the eyes. It has been shown that the periphery of the retinas does, indeed, significantly contribute to the act of fusion in people with normal binocular vision (Burian, Arch. Ophth. *21:* 486, 1939; Ogle, Researches in Binocular Vision, Saunders, 1950). More especially the proper alignment of the vertical and horizontal meridians, i.e. the prevention of cyclodeviations, must depend on the retinal periphery. Patients with manifest strabismus may also show fusional movements elicited by stimuli applied to the retinal periphery, although these patients show a variety of patterns of behavior with respect to their responsiveness to peripherally and centrally presented fusional stimuli (Burian, Arch. Ophth. *26:* 626, 1941). It is on the basis of these differences in behavior that new approaches to orthoptic techniques might be evolved (Burian, Am. J. Ophth. *30:* 1005, 1947). A very strong peripheral fusional stimulus may also overcome the fusional attraction of a small centrally fixated pattern, simply because of the discrepancy in the strength of the central and peripheral stimuli, and this in spite of the attention value of the centrally fixated object and of the enormous magnification of the retinal fovea in the calcarine cortex.

Lyle and Foley have now confirmed the presence of peripheral fusion with varying degrees of peripheral suppression, but have found their results to be varied and inconclusive owing to the subjective nature of the tests which they used. It seems that they requested a report from their subjects as to whether or not they had diplopia or saw singly, either centrally or peripherally.

The experimental arrangement used by Lyle and Foley differed in an important respect from the one used by Burian. In Burian's set-up the patient was presented with two short horizontal lines, one seen by each eye, which he fixated and one of which was movable. Occasionally a small binocularly seen central object was added for special purposes. The task of the observer was to keep the movable horizontal test-line so adjusted that it appeared to him at all times to be opposite the fixed test line. The experimenter inferred from the objective position of the test lines on the screen whether or not certain fusional stimuli, applied to different parts of the retina resulted in fusional movements of the eyes or not. Comments of the observer—spontaneous or in response to question—were only used to corroborate the findings and measurements. The observer's contribution was thus restricted to his willingness and ability to fixate on the test lines and to keep them aligned. This reduced the subjective factor to a minimum.

It is to be hoped and expected that further studies of the differences in behavior of the central and peripheral retinal areas in patients with strabismus may contribute to the knowledge of the visual act of squinters and to the advance of orthoptic techniques. The modification of the Pigeon-Cantonnet stereoscope, cleverly devised by Lyle and Foley will doubtless contribute to this end.

HERMANN M. BURIAN

A PLEA FOR THE EARLY TREATMENT OF STRABISMUS

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Detroit, Michigan

Harper Hosp. Bull. 1955, *13:* 147–149

The cause of strabismus is always an obstacle, anatomic, innervational or psychologic, which interferes with normal reflex development. To prove that strabismus can be functionally cured, only by removing such an obstacle before abnormally developing reflexes become fixed, the authors analyzed 382 cases of concomitant convergent strabismus, which came to surgery. They wished to establish the relationship between age at the time of surgery and the end result. A functional cure was defined as showing absence of tropia on cover for both near and far, fusion of Worth four dots for near and far, fusion of the red glass for near and far, equal vision in the two eyes and absence of muscle weakness.

TABLE 1

Non-Accommodative Comitant Esotropia

Group	Age in Years	Number of Cases	Fusional Result			Cosmetic Result		
			Surgery only	Surgery and orth-optics	Percent of cases	Surgery only	Surgery and orthoptics	Percent of cases
I	0–3	78	26	2	35.9	37	13	64.1
II	4–5	114	16	23	34.2	42	33	65.8
III	6–7	68	2	16	26.5	21	29	73.5
IV	8–12	62	2	8	16.1	24	28	83.9
V	12+	60	6	3	15.0	44	7	85.0
Total.....		382	52	52	27.2	168	110	72.8

The results are shown in Table 1. Of all cases treated surgically, 27.2 per cent were functionally cured. Cases complicated by a high vertical anomaly, anisometropia, and intractable amblyopia were included and thus the results are not unsatisfactory. It was evident that the percentage of successful results was higher in patients operated upon before the age of six years and that the number of successful results diminished in each successive age group.

Comment: The need for early treatment of patients with strabismus, has been frequently emphasized in recent years, and there can be no doubt, that some form of treatment can be instituted at any age, although not all forms of treatment are suitable for patients of every age.

With regard to surgical treatment the present trend is toward early surgery to afford the child the benefit of growing up with properly positioned eyes. The question remains open, however, in regard to the earliest age at which a child should be operated upon. There are many factors, which determine the best course of action, in each individual case. The severity of the squint and of the refractive error are among them; some surgeons prefer to postpone operation until the child is old enough to permit them to gather

information, which they consider pertinent, in making a surgical decision. The normal "drift" of the eyes from an eso- to an exoposition during the years of childhood and early youth—due possibly to a reduction in tonic convergence innervation—must also be taken into consideration. If it is true, that in some cases of strabismus, at least a retardation or deficiency of the development in some nervous structures is at the root of the matter, a very early straightening of the eyes (prior to the age of 18 months or 2 years) would not seem to be particularly helpful in insuring a functional result.

In connection with all these unresolved problems it is of interest to note from the table presented by the authors that with respect to the functional result attained there is no appreciable difference between the group of patients operated upon between 0–3 years and the group of patients operated upon between 4–5 years of age. It certainly remains true that early operation is desirable, but the disadvantages of very early operation may well overshadow the advantages in the ordinary cases.

HERMANN M. BURIAN

THE INTRAOCULAR PRESSURE

PRIMARY DEGENERATION IN THE VICINITY OF THE CHAMBER ANGLE AS AN ETIOLOGIC FACTOR IN WIDE-ANGLE GLAUCOMA

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Eye-Bank for Sight Restoration, New York, New York

Am. J. Ophth. 1955, *40:* 619–631

Studies of histologic sections of 2,792 eyes in the Eye-Bank indicate 10.4 per cent with a degeneration of the angle not previously reported. This change is most frequently found in the external portion of the trabecula where the fibers are usually thinner and arranged more compactly. It spreads along collagen fibers either externally or internally to the walls of Schlemm's canal, to the collector channels and even to the intrascleral plexus.

The degeneration initially causes the ground substance of the collagen to break down into granules and then disappear. Elastic fibers are more resistant than collagen but also degenerate eventually. In the trabecular region after degeneration of the collagen and elastic fibers the endothelial cells proliferate to form an edematous, spongy mass or a laminated membrane.

These changes cause an increased resistance to outflow of aqueous or decreased facility of outflow because of one or several processes. The loss of collagen causes a collapse of the trabecular network and obliteration of the trabecular spaces. The lumen of Schlemm's canal may be decreased because of adhesions between the inner and the outer wall. In the most serious form of obstruction, the collector channels may be occluded, because of proliferation and swelling of their endothelium, or because of distortion with obliteration of their lumen.

In three patients with known early wide-angle glaucoma this degeneration was present in an extensive and advanced form. The cause is unknown but it may be due to one or more proteolytic enzymes or due to a dissolution process. The studies suggest that wide-angle glaucoma is a degenerative disease involving the wall of the chamber angle.

Comment: The work of these authors appears at a time when considerable attention is being focused on the question of the site of the resistance to outflow of the aqueous humor in eyes with simple open-angle glaucoma. The question became controversial during the days of the earlier gonioscopic observations and has continued. There are those who believe they can recognize variations in trabecular transparency clinically and call it trabecular sclerosis. Others cannot recognize any difference from the normal gonioscopically.

Van Beuningen (v. Graefe's Arch. f. Opht. *156:* 35, 1954) studied the density of the trabeculum with Goldmann's slit-lamp tyndallimeter and found greater density of the

trabeculum in eyes with primary glaucoma than in normal eyes and concluded that marked density of the trabeculum may point to the presence of glaucoma.

Experimentally, Bárány has shown that the resistance of the trabeculae in the trabecular wall to outflow of aqueous humor can be reduced by approximately one-half in enucleated chicken eyes by the addition of hyaluronidase. He advanced the theory that the responsible sensitive material in the trabeculum is hyaluronic acid in the polysaccharide gel lining the surface of the trabecular meshwork. Goldmann and Linner also believe the trabeculum to be the site of resistance to aqueous outflow.

On the other hand Ascher considers, from aqueous vein studies, that the site of resistance is in the collector channels leading from Schlemm's canal. Grant, in enucleated human eyes, found the site of resistance to be between Schlemm's canal and the outer half of the sclera.

We must, therefore, conclude that the problem of the site of resistance to aqueous outflow has not been solved but there is certainly a good deal of evidence in favor of the trabeculum.

Although the authors state that "Decreased facility or increased resistance to the outflow of aqueous results from these pathologic processes", this has actually not been proven. One can only say that a hitherto unrecognized change in the trabeculum has been observed in nonglaucomatous eyes and may be of importance etiologically.

H. Saul Sugar

PERIPHERAL IRIS CRYPTS IN RELATION TO MEDICAL AND SURGICAL THERAPY OF NARROW-ANGLE GLAUCOMA

Adolph Posner

New York, New York

Am. J. Ophth., 1955, *40:* 469–474

Closure of the angle of the anterior chamber, which accompanies elevation of intraocular pressure in narrow-angle glaucoma, is caused by circumferential contact between iris and cornea. This contact, or iris block, occurs initially at the entrance to the angle and is found almost exclusively in eyes in which the entrance is anatomically so narrow that further narrowing leads to embarrassment of the aqueous circulation. Lowering of the pressure, either spontaneously or as a result of medical treatment, is followed by reopening of the angle. Attempts to explain iris block as a crowding of the angle by iris tissue (as in "dilation glaucoma"), or as a swelling of the ciliary body, or as a forward displacement of the lens, are not entirely satisfactory, because they are inconsistent with the fine results obtained by a small peripheral iridectomy which leaves the root of the iris intact and merely establishes a communication between the posterior and anterior chambers. Both the mechanism of the acute attack and the curative

action of iridectomy in narrow-angle glaucoma, however, can be explained by the iris suction theory. According to this theory, circumferential contact between iris and cornea at the entrance to the angle prevents aqueous from reaching the peripheral zone of the anterior chamber. The aqueous contained in the peripheral zone soon drains off and the root of the iris is held against the trabecula by suction from Schlemm's canal, where the pressure is relatively low. The normal hydrostatic pressure in Schlemm's canal and the episcleral veins is about 10 mm. Hg, while the pressure behind the iris, represented by the intraocular pressure, is 20 mm. Hg. In the absence of aqueous in front of the iris to equalize the pressures, the iris assumes a convex shape referred to as "physiologic iris bombé." Since the drainage channels are blocked by the iris's being held against the trabecula, the pressure in the posterior chamber rises as a result of both the continuing formation of aqueous and the osmotic imbibition of water by the already formed aqueous. The permanent communication established by iridectomy between the posterior chamber and the periphery of the anterior chamber equalizes the pressures between them and thus eliminates the cause of the acute attack.

Two questions, however, still remain to be answered. 1. Since the width of the angle is the same in both eyes, why do many persons suffer from recurrent attacks of narrow-angle glaucoma in one eye only, while the other eye is either completely or relatively free from attacks? 2. An anatomically narrow angle, which is apparently an inherited characteristic, is present in about 10 per cent of the random population. Why, then, does narrow-angle glaucoma develop in less than 1 per cent of the population, and why, even in persons with a narrow angle, do many years sometimes elapse before symptoms of glaucoma become evident?

The answer to these questions may perhaps be found in a simple mechanical process. Closure of the angle presupposes the formation of a watertight barrier between the central and peripheral zones of the anterior chamber. A defect in the anterior surface of the iris, such as a pit or crypt, when suitably placed, may create a leak in the barrier, so that communication between the center and periphery of the anterior chamber is assured and the eye is safeguarded against glaucomatous attacks. Observations on many patients have shown, first, that in eyes exhibiting clinical symptoms of narrow-angle glaucoma, the peripheral zone of the anterior leaf of the iris stroma is usually smooth and presents an unbroken surface; and, second, that in many instances of unilateral narrow-angle glaucoma, the iris of the normal fellow eye is pitted by well-circumscribed peripheral iris crypts. These crypts vary in size and number and are usually located just central to the limbus. Their peripheral position accounts for the fact that they are not generally accessible to slit-lamp examination. Gonioscopy, too, fails to reveal them, because they are usually hidden from view by the last roll of the iris.

The author's studies suggest that eyes with narrow chamber angles, in which peripheral iris crypts are not visible with the slit-lamp, may be subject to acute attacks of glaucoma. Conversely, eyes with well-developed peripheral iris crypts, which are sometimes visible on slitlamp examination, usually have no history of glaucoma and are not subject to elevations of tension even though the chamber angle is narrow.

Other factors that affect the susceptibility of a narrow angle eye to glaucomatous attacks are density of the iris stroma and the degree of development of radial and circular furrows. These markings of the anterior surface of the iris tend to become less pronounced with advancing age. The resulting smoothness of the iris, coupled with the decreasing depth of the anterior chamber usually associated with growth of the lens, may account for the increased frequency of acute glaucoma in older persons.

The most conservative, as well as the most effective method of preventing recurrences of acute narrow-angle glaucoma is a peripheral iridectomy. Observations of iris crypts tend to confirm the belief that iridectomy is the operation of choice in this condition, even when it has existed for years. Only when the tension is consistently elevated or several congestive attacks have already occurred is iridencleisis necessary.

Comment: This intriguing theory requires corroborative observations which, as Posner states, cannot be made gonioscopically due to the concealment of the crypts by the last roll of the iris. Several points might be made in evaluating the theory. First, one might compare the incidence of acute angle-closure glaucoma in blue eyes and in the dark-brown eyes of Negroes. The texture of the anterior iris surface in these two types differs considerably. Many crypts are usually found in light blue irides while the surface is smoother and contains few crypts in the dark brown irides. There is no evidence to date of any significant difference in incidence according to iris color. Second, the incidence of unilateral acute glaucoma may depend on variations in the anterior chamber and angle depth of the two eyes rather than on the crypts. Thus it is often found that in patients with high hyperopia but with considerable difference between the two eyes, perhaps enough to cause amblyopia in the eye with the highest error, the acute attack often occurs first in the amblyopic eye, later in the other eye.

Winter has shown elsewhere in this issue that a considerable time may elapse between the attacks in the two eyes. Sixty-eight per cent of 47 cases had an acute congestive attack in the second eye within 5 years of the first attack in the first eye.

A third observation is that the normal iris is thin and sufficiently malleable that crypt edges would be defaced by any pressure against the trabeculum.

A fourth observation involves the question of peripheral iris atrophy acting like a peripheral iris crypt. It may be suggested that extensive iris atrophy may be associated with scar tissue formation which tends to keep the iris relatively immobile and may prevent further attacks in those associated with pupillary dilatation and may splint the iris in other cases. This splinting, plus destruction of portions of the sphincter, may prevent pupil block.

These observations should be considered in studies which aim at corroborating this interesting paper.

H. Saul Sugar

THE SECOND EYE IN ACUTE, PRIMARY, SHALLOW-CHAMBER ANGLE GLAUCOMA

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Am. J. Ophth., 1955, *40:* 557–558

A study was made of the fate of the second eye in 47 cases of acute congestive shallow-chamber angle glaucoma, in which the second eye was normal at the time of the initial attack. The cases studied were selected from about 1000 histories of glaucoma patients seen at the Wilmer Institute, The Johns Hopkins Hospital, between 1939 and 1949. Only cases representing primary shallow-chamber angle glaucoma were included in the study and all had to meet the following criteria: (1) An acute congestive attack in the first eye with initial tension over 60 mm. Hg (Schiotz); (2) a specific notation in the chart that the anterior chamber angle was shallow in each eye, either by slitlamp or gonioscopic examination; and (3) tension in the second eye normal at the time of the first admission and no history of previous attack in that eye.

TABLE 1

Effect of Prophylactic Miotics on the Second Eye in Acute Congestive, Primary, Shallow-Chamber Angle Glaucoma

Miotics	Number of Cases	Number Having Attack in Second Eye	%
Continuous	20	8	40
Intermittent	8	7	88
None	19	17	89

Study of the histories in these cases showed that an acute congestive attack occurred in the second eye of 32 patients (68 per cent). The time interval between the attack in the first eye and that in the second varied from a minimum of a few hours to a maximum of 18 years. In 29 cases (62 per cent), however, the attack in the second eye occurred within 5 years of that in the first eye. The age of the patient did not appear to influence the susceptibility of the second eye to an attack of acute congestive glaucoma. Once an attack had occurred in the first eye, the patients were equally susceptible to one in the second eye at all ages.

Preventive treatment may consist of the continuous use of miotics or a prophylactic peripheral iridotomy. A review of the use of miotics, in these patients, showed that 27 took them intermittently or not at all and that of these 89 per cent had an attack in the second eye. The frequency of attacks in the second eye in patients who took miotics continuously was less than half as great (40 per cent of 20 patients) as that in those who were untreated or poorly treated. The fact that 62 per cent of the attacks in the second eye occurred within 5 years of those

in the first eye suggests that prophylactic peripheral iridotomy, which is strongly advocated by some authorities as a more effective preventive measure than the use of miotics, is especially indicated in the younger patients.

Comment: The occurrence of an attack of acute glaucoma in the second eye in 40 per cent of patients who used miotics continuously certainly suggests the use of prophylactic peripheral iridectomy. The decision as to whether to continue the use of miotics or to operate depends on several factors: 1) the dependability of the patient in using miotics, 2) the age of the patient, 3) the geographic availability of surgical treatment and 4) the psychologic threat of recurrent attacks on the patient. One must also remember that in spite of the excellent prognosis with surgery, the possibility of surgical complications always exists.

H. Saul Sugar

SYMPTOMS OF CONGESTIVE (CLOSED-ANGLE) GLAUCOMA OCCURRING IN EYES WITH A WIDE CHAMBER ANGLE

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Brit. J. Ophth., 1955, *39:* 673–680

Modern methods of examination, especially the use of the gonioscope, now enable us to divide the primary glaucomas into two distinct conditions differing in cause, symptoms, prognosis, and treatment. Closed-angle glaucoma, previously referred to as congestive glaucoma or narrow-angle glaucoma, may occur at any age, but typically affects younger people than does chronic simple glaucoma, especially when congestive attacks, apparently, due to increase in the size of the lens are discounted. Usually, the symptoms are easily recognizable: the condition manifests itself either as an acute attack, or as a series of minor congestive episodes gradually increasing in severity until an acute attack occurs or until organic changes take place in the angle of the anterior chamber and the disease enters a chronic phase. The characteristic symptom of the early congestive attacks is misty vision and the appearance of haloes around lights, occurring typically when the patient is tired or worried, in the evening, especially after watching the cinema or television, or occasionally after reading.

Simple glaucoma, on the other hand, is a disease of insidious onset, seldom producing any subjective symptoms in the early stages. It can occur at any age, but is most common in patients over 60. Haloes are said to occur very rarely in simple glaucoma and then only when the disease is in a late stage, although they have occasionally been found in cases of early simple glaucoma. The reports of gonioscopy findings have further strengthened the division between the two types of glaucoma. The angle in simple glaucoma is usually medium or wide and

the depth of the anterior chamber normal. This, however, is not always the case, as the angle can be of any width varying from wide to narrow, as in the normal eye. The term "wide-angle" glaucoma is thus misleading, and the term "normal angle width" should be used for glaucoma simplex if a gonioscopic classification is desired.

Closed-angle glaucoma is associated, almost invariably, with a narrow chamber angle and a shallow anterior chamber. An angle narrow enough to become blocked is the essential feature of congestive glaucoma, and if gonioscopy fails to reveal this condition, the diagnosis is excluded. While it is true that a narrow angle is usually associated with a shallow anterior chamber, this is not always the case, and as a result glaucoma can be classified only by gonioscopy.

From the evidence available, it seems probable that simple glaucoma is caused by a permanent obstruction to the outflow of aqueous leading to vascular changes that ultimately produce a permanent rise in tension. The lack of gonioscopic evidence of any change in the filtration angle suggests that this obstruction is situated in the intrascleral vessels draining Schlemm's canal. Closed-angle glaucoma, on the other hand, is usually associated with a narrow angle, and attacks are believed to be due to sudden blocking of this angle by the iris root. These differences in etiology naturally lead to differences in treatment. In simple glaucoma, the facility of aqueous outflow from Schlemm's canal must be increased, either by the use of miotics to lower the episcleral venous pressure, by the surgical construction of new drainage channels, or by diminishing the secretion from the ciliary body. In closed-angle glaucoma, the attacks of high tension can be prevented by treatment designed to keep the root of the iris from blocking the angle. This may be done by miotics or with a basal iridectomy, either peripheral or complete; filtering operations are necessary only when permanent changes have occurred in the angle.

The type of glaucoma must therefore be established before any method of treatment is decided upon. At first sight, this may appear comparatively simple, but because the attacks of haloes and misty vision which are symptomatic of narrow-angle glaucoma may also occur in the presence of a wide or medium angle, the ophthalmologist may be misled into performing simple iridectomies on patients in whom such operations have no chance of success. The importance of the differential diagnosis is illustrated by four types of cases, in all of which the patients had symptoms which could be considered typical of congestive glaucoma, but which differed from it in several essential features quite apart from the gonioscopic findings.

In the first patient, a 27-year-old man, a rise in tension was accompanied by signs of inflammation so slight that the glaucoma seemed to be entirely disproportionate. The suggestion has been made that this condition lies between true primary glaucoma and the secondary glaucomas, inasmuch as the rise in tension is not secondary to the inflammation, but both the glaucoma and the cyclitis have a common cause, possibly allergy. It may be, however, that cyclitis can cause vascular changes in the uveal tract and intrascleral vessels, and that these changes may lead to an increased rate of formation of aqueous by the ciliary body as well as partial obstruction of aqueous outflow. In this condition, the eyes

will be completely normal between attacks; all provocative tests will be negative, and the angles will be found to be normal. Therefore, when a patient reports misty vision and haloes but neither gonioscopy nor provocative tests support the diagnosis of narrow-angle glaucoma, the possibility of glaucomato-cyclitis crises must be considered.

In each of the other three types of cases, the congestive symptoms presented were such that mistakes in diagnosis might easily have been made had it not been for the fact that gonioscopy disproved the existence of angle block.

These observations are not presented for the purpose of disputing the fact that angle block is the cause of closed-angle glaucoma, but merely to show that the belief that intermittent attacks of misty vision with or without haloes are symptoms entirely confined to congestive narrow-angle glaucoma is not entirely correct.

Comment: This paper serves to emphasize the fact that some of the symptoms usually associated with congestion may occur in simple glaucoma. Evidently the occurrence of such symptoms is related not to the height of the ocular tension but to the rate of increase of the latter.

Blaxter uses a case of glaucomato-cyclitic crises as an example of wide angle glaucoma. This condition is a form of secondary glaucoma. Many other types of secondary glaucoma with open angles, especially with iridocyclitis may give the same symptoms. Here again the rapid increase of intraocular pressure is probably the cause. The successful use of atropine in this case to lower the tension emphasizes the cyclitic nature of this disease and emphasizes its position as a secondary glaucoma.

H. Saul Sugar

THE THALAMOCORTICAL PATHOGENESIS OF GLAUCOMA: A NEUROPSYCHIATRIST ATTEMPTS AN INCURSION INTO THE DOMAIN OF OPHTHALMOLOGY

Radovici

Bucharest, Roumania

Ann. ocul., 1955, *188:* 881–903

The failure of all the theories previously advanced, to explain the pathogenesis of glaucoma, may be traced to the fact that glaucoma has been considered a purely ocular condition and its cause has been sought solely in the eye itself. The functions of the brain, or, in the language of Pavlov, the psychic state, especially the emotions, have been proved to play an important part in the pathogenesis of glaucoma and in the precipitation of acute attacks. Psychosomatic medicine has for a long time almost completely neglected the eye, which has been regarded as under the rule of exact physical laws and only very slightly susceptible to psychic influences.

Increasing awareness of the regulatory influence exerted by the cerebral cortex and the diencephalon, on our reactions to external circumstances, has in the last few years, naturally, led ophthalmologists to attribute to the diencephalon, that is, to the thalamus and the hypothalamus, an important part in the regulation of ocular tension. Clinical and experimental studies by Magitot and various Soviet investigators have provided evidence in support of this reasoning, although it has still to be confirmed by histopathological studies of the brains of glaucomatous subjects. The absence of lesions, or their insignificance, would not, however, exclude the possibility of participation by the diencephalon in the production of glaucomatous hypertension, any more than the absence or insignificance of cerebral lesions in epilepsy excludes the participation of the brain in the appearance of epileptic crises.

While it is true that neither the diencephalic lesion nor the humoral factor responsible for primary glaucoma has yet been identified, there are many concordant clinical and physiopathological findings tending to show that the principal site of the glaucomatous disturbance is to be found in the hypothalamus, the nuclei of the tuber, the infundibulum, and the hypophyseal gland, which is synergistic with these centers. According to Magitot, the patient with glaucoma is "thalamically hypersensitive." This "explains the anxiety, the influence of emotional shock, and the pathological fear frequent in glaucomatous subjects. This is why emotional, thermal, or painful disturbances may precipitate an acute attack. This explains the vegetative hypersensitivity, the vasomotor reactions, and the obliteration of the capillaries in persons with glaucoma. The dysfunction of the same thalamo-hypothalamic regions provides the reason for the disturbances in water metabolism, pupillary disorders, and post-hypophyseal endocrine dystony characteristic of glaucoma."

This concept, which goes beyond the problem of glaucoma attributed to a simple mechanical obstacle, raises the question to a higher level and transforms glaucoma into a systemic disease. The value of the new concept of the diencephalic origin of glaucoma is not merely theoretic but practical, because it leads to certain changes in the treatment of the disease. First, in every case of glaucoma, the ophthalmologic examination should be supplemented by a neuropsychiatric investigation. All attempts at prophylactic treatment may prove deceptive unless an effort is made simultaneously to remove the cause of the underlying anxiety and the psychic conflicts responsible for the condition. In addition to medications and operations, the patient with glaucoma must be given advice about his manner of living, his work, avoidance of overfatigue, cultivation of tranquillity, and the like. Many of the changes recommended may be difficult to put into effect, but the effort should be made and the patient warned that his sight depends upon their successful accomplishment.

For therapy, the barbiturates are no less important than pilocarpine. These substances, which are the specific sedatives of the diencephalic centers, provide real help in the early stages of the disease. They should be given daily for months or even years, just as they are in the case of epilepsy or essential hypertension. The particular barbiturate to be used for each patient should be selected, and the dosage adjusted, to provide sedation of nervousness and anxiety without

producing somnolence. A single dose at bed-time is probably preferable to divided doses given throughout the day. Even in acute attacks fistulizing operations on the eye can often be avoided. The judicious use of general anesthesia, especially pentothal sodium given intravenously, always produces a drop in tension, while at the same time a retrobulbar injection, under anesthesia, of 60° alcohol will check the painful crisis of acute glaucoma. Sometimes, in subacute crises, a retrobulbar injection of 5 per cent procaine alone is sufficient.

The treatment of chronic glaucoma, which is designed to arrest the disease and prevent blindness, must, of course, be purely medical; it can succeed only in the early stages, being entirely without effect in the terminal stage.

Comment: The question of the diencephalic control of the intraocular pressure has been a matter of conjecture for many years. At present experimental studies are being carried on to arrive at some conclusions regarding the presence and degree of such control. This paper by a Bucharest neuropsychiatrist, influenced by Magitot particularly, gives the theoretical background for the European ideas about this subject.

As to a diencephalic control of vessels in the eye, particularly the blood retinal vessels, there is ample experimental evidence. We can also assume that changes in the rate of formation of aqueous in the unmedicated eye depend largely on the vascular system. That these vessels can be affected by nervous and psychic influences is to be expected. However, we are at present, more concerned with resistance to outflow of aqueous, and there is no proof of the diencephalic control of outflow. Certain suggestions of some reflex control through the central nervous system are evident, however. Among these are the evidence that application of a tonometer to one eye for four minutes during tonography causes a lowering of the tension in the fellow eye. Clinically the successful reduction of tension by surgery in one eye often favorably affects tension in the other eye.

One could disagree with Radovici concerning his evidence from "incomplete glaucoma", or really pseudoglaucoma cases, which are not glaucoma at all. His statement that operations might be avoided in acute glaucoma by giving general anesthesia and a novocaine-alcohol injection does not fit in with our ideas of acute angle-closure glaucoma.

The suggestion that treatment of simple glaucoma consists of miotics, sedatives and prevention of untoward psychic stimuli should be followed by more ophthalmologists.

H. Saul Sugar

THE LIMITS OF PHYSIOLOGICAL OCULAR PRESSURE

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Ann. ocul., 1955, *188:* 920–926

In order to determine the limits of physiological ocular pressure, under the new conditions of examination established by the American 1954 calibration

scale, for Schiotz tonometers, tonometric measurements were made in 390 normal subjects without a glaucomatous background and without significant ametropia. Measurements made under difficulties, e.g., blinking, blepharospasm, unsteadiness of gaze, and the like, were excluded. A European tonometer conforming to the American standard was used for 300 of the measurements; the other 90 were made with an American tonometer of recent design.

From the findings, it appears that the values of physiological ocular pressure are the same for different tonometers if the instruments are in strict conformity with the American standards. The values also agree perfectly with those established by Goldmann with the new applanation tonometer. In all probability, they are an exact measure of the intraocular hydrostatic pressure.

Age apparently has little, if any, effect on the ocular pressure. This point, which is at variance with earlier findings, requires further study in patients in the older age groups. The range of the physiological ocular pressure extends from 10 to 22 mm. Hg. This wide range makes it difficult to determine the physiological limit for a given person. A pressure above 22 or 23 mm. Hg is certainly pathologic. One in the neighborhood of 21 or 22 mm. Hg should be viewed with suspicion, and one of from 20 to 21 mm. Hg cannot be definitely stated to be normal, since it may represent a pathologic increase over one that was previously lower.

In the light of these facts, it appears that most cases of glaucoma "without hypertension" are glaucoma with slight hypertension. The actual existence of glaucoma without hypertension is not a certainly. It has, on the other hand, been amply shown, that a very slight hypertension, of the order of from 2 to 3 mm. Hg, may, in the course of several years, produce significant defects in the usual field. This conclusion, which seems to be well established, is theoretically important because it emphasizes the part played by hydrostatic disturbances in the pathogenesis of glaucoma, and in addition it has a special practical bearing on the treatment of glaucoma.

A 5.5 gr. weight was used in making the measurements in this study. In everyday clinical practice, the 7.5, 10, and 15 gr. weights are used only in cases of hypertension. The possibilities of error seem to justify the choice of a weight great enough to give a deviation of at least three graduations. The form of the tonometric curves is such that an error in reading on the tonometer scale leads to an error in the ocular pressure measurement that is all the greater the less the deviation.

Comment: As a result of the adoption, by the Committee on Standardization of Tonometers of the American Academy of Ophthalmology and Otolaryngology, of a new calibration scale in 1954, the values for the normal must be re-interpreted for each ophthalmologist and each tonometer. The average normal readings are lower, corresponding to 15 to 18 mm.

As part of the process of making the new scale universal, Weekers and his associates have studied a series of 300 normal patients with a European-make tonometer and 90 with the American-made instrument. The values were the same and averaged approximately 16 mm., in accord with Goldmann's findings with his applanation tonometer.

The physiologic limits were found to be 10–22 mm. Hg. With these values 21–22 mm. are considered suspect and 22–23 pathologic. These values were all determined using the 5.5 gm. weight. It is at this point particularly, where the tension value becomes suspicious that difficulty arises. The only conclusion one should reasonably draw is that the normal limits for the individual tonometer and observer should be determined by experience with a series of perhaps 25 relaxed normal patients.

Age apparently has little effect on the physiologic tension limits according to the authors but they point out that tonography and fluorimetry indicate a slight increase in resistance with age. Since we are dealing here with normals, there is enough leeway so that the tension is unaffected.

H. Saul Sugar

DELAYED FORMATION OF THE ANTERIOR CHAMBER: A SIMPLE METHOD OF TREATMENT

T. M. Armstrong

Sidney

Trans. Ophth. Soc. Australia, 1954, *14:* 117–118

Delayed formation of the anterior chamber especially after glaucoma operations is a serious threat to the eye. Cataract, hypotony and corneal opacities are frequent sequelae. The condition is due to a leaking wound. A method based upon that of Town and Naidoff (Amer. J. Ophth. 1950, *33:* 879) and Tassman (Amer. J. Ophth. 1950, *33:* 870) using fibrin closure of wounds was used in 12 cases of delayed formation of the anterior chamber.

Plasma is obtained by centrifuging the small amount of blood remaining in transfusion bottles. The eye is anesthetized and a few drops of plasma placed over the site of incision and then one or two drops of "Thrombin Topical." The eye is left open for one or two minutes to allow the clot to become firm and then closed gently, the upper lid being lifted over the clot so as not to dislodge it. In all 12 cases in which this method was used the anterior chamber was reformed 24 hours later.

Comment: This brief article is rather ambiguous. The author discusses the delayed formation of the anterior chamber following filtering operations for glaucoma and believes that this is due to a leaking wound. In the discussion, he states that most of the cases, twelve in number, were cases in which an Elliott trephine operation had been performed. Delayed formation of the anterior chamber following a trephine operation has been known for many years and is one of the known drawbacks of performing the operation. This need not necessarily be due to a leaking wound but to a marked filtration through the trephine opening. It is well known that some trephine openings appear to drain much more readily following operations than others. If a good filtering bleb is present,

it is hardly possible to abscribe the shallow anterior chamber to a leaking wound since that is what is attempted with the operation. However, if no filtering bleb is seen, and the chamber is shallow, one must assume that there is a break in the continuity in the conjunctiva at the limbus and there is a direct opening from the eye to the corneal surface. Providing this is the case, the use of fibrin, as suggested by the author, might be of some advantage. No mention is made in the article as to whether a fluorescein test was done to see if there was a leak in the wound at the site of the conjunctiva over the trephine opening or whether the wound was leaking from the conjunctival incision. Properly, this incision should be placed 6 or 8 mm. from the limbus and should be sewed fairly firmly. It is very unusual for aqueous to escape in this area if the conjunctiva is closely approximated. Slip lamp examination of these cases will very frequently reveal a very small dehiscence in the conjunctiva immediately over the trephine opening. This, of course, should be avoided, and the only way to do it is meticulous disection of the conjunctiva, being careful not to buttonhole it and to include Tenon's capsule in the limbal base flap if at all possible.

P. Robb McDonald

NEUROLOGY

OPHTHALMOLOGIC CHANGES PRODUCED BY PITUITARY TUMORS

MAX CHAMLIN, LEO M. DAVIDOFF, AND EMANUEL H. FEIRING

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Am. J. Ophth., 1955, *40:* 353–368

The diagnosis of pituitary adenomas and craniopharyngiomas is greatly facilitated by an understanding of the ophthalmologic changes they produce. Ophthalmologic study of 156 patients selected on the basis of evidence indicating the existence of a pituitary adenoma or craniopharyngioma showed the following common and uncommon signs, listed in the order of their frequency: (1) Visual field defects, (2) atrophy of the optic disks, (3) loss of central vision, (4) extraocular muscle palsies, (5) pupillary changes, (6) involvement of the trigeminal nerve, (7) papilledema, and (8) proptosis; in none of these cases was nystagmus present. Only patients with chromophobe adenoma, eosinophilic adenoma, craniopharyngioma, and a basophilic state were included in the study, and since the purpose of this report is to stimulate the earliest possible diagnosis of such lesions, the data presented are always the earliest available for each case. In some of the patients, however, the disease was already in a late stage when the first examination was made, so that the first information obtained gave evidence of advanced changes. In 71 instances, the nature of the tumor was verified surgically. In some of the others, pneumoencephalography confirmed the presence of a mass rising from the sella turcica.

Visual Field Defects. The most constant and classic type of visual field defect in pituitary tumors, i.e., bitemporal hemianopsia, appeared in one form or another in 134 of the patients (86 per cent). In a good many cases of eosinophilic adenoma, the visual fields may remain unaffected; 15 of the 23 patients in this series whose lesions were eosinophilic showed normal fields. Moreover, the picture of acromegaly produced by these tumors is usually so classical that discovery of visual field defects is not needed for confirmation of the diagnosis. In basophilism, or Cushing's syndrome, too, the clinical picture is quite typical and the visual fields are hardly ever affected. The situation, however, is quite different in the case of chromophobe adenomas and craniopharyngiomas. Thus, in this series, the incidence of bitemporal hemianopsia in the 109 patients with chromophobe adenomas was 96 per cent and in the 18 with craniopharyngiomas it was 100 per cent. Roentgenographic evidence is often very helpful, but in a number of cases of chromophobe adenoma and craniopharyngioma no significant changes could be seen in the sella turcica and pneumoencephalography had to be utilized in order to prove the existence of a mass which had been suggested by

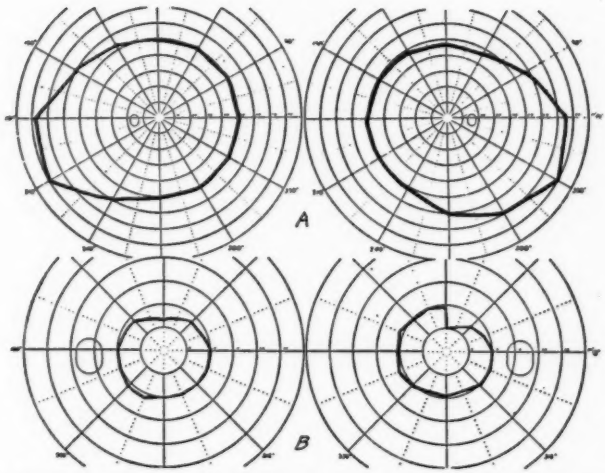

FIG. 1. (Chamlin, Davidoff, and Feiring). A. F., a 17-year-old white youth with craniopharyngioma, verified surgically. No visual complaints. Visual acuity 20/20 in each eye. A. Peripheral fields for 2/250 white completely normal. B. Fields for 1/2000 white showing definite upper temporal hemianoptic defect in right eye. (Reproduced with permission, American Journal Ophthalmology).

the presence of bitemporal hemianopsia. The high incidence (100 per cent) of bitemporal hemianopsia found in the 18 patients here considered may have been due to the fact that they were subjected to sensitive types of minimal testing; some of the visual field defects observed were, in fact, very slight and might easily have been missed with other types of testing. In almost all cases of chiasmal interference the indication of this defect is first found in the 1/2000 field, and this field usually shows as much of the defect as does the peripheral field. This has been borne out by studies of numerous cases in many of which the peripheral fields remain completely normal while the 1/2000 fields show bitemporal defects (Figs. 1 and 2). The 1/2000 field may show evidence of a bitemporal defect for many months before the central visual acuity, as measured on the Snellen chart, is affected.

One of the major problems of differential diagnosis relates to retrobulbar neuritis, which is often confused with chiasmal interference. Care must be taken to ascertain whether the visual field defect present fits into one of the categories found in cases of retrobulbar neuritis, namely, caecocentral scotomas, and/or paracentral scotomas emanating as nerve-fiber bundle defects from the blind-spot. The discovery of hemianoptic features in a patient thought to have retrobulbar neuritis should be considered indicative of chiasmal interference, and if such interference can be demonstrated, it should be considered due to tumor until proved otherwise.

Optic atrophy, which eventually appears in eyes that show bitemporal hemianopsia, was indicated by pallor of the disks in 155 (50 per cent) of the eyes

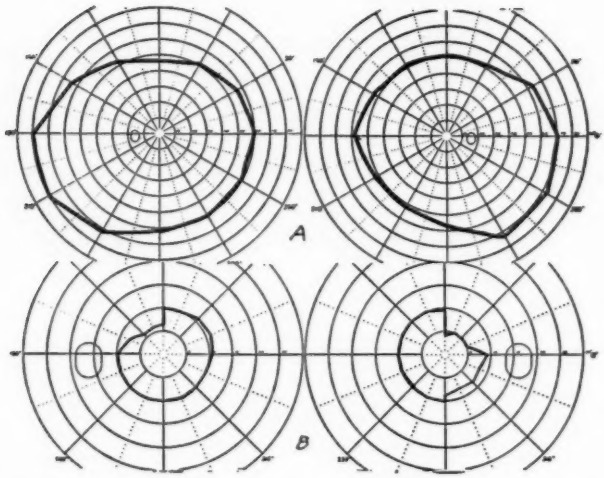

Fig. 2. (Chamlin, Davidoff, and Feiring). W. R., a young white man with craniopharyngioma, verified surgically. Complaint of blurring in right eye only. Vision, right eye, 20/70; left eye, 20/30. A. Peripheral fields for 2/250 white completely normal. B. Fields for 1/2000 white showing bitemporal hemianoptic defect. (Reproduced with permission, American Journal Ophthalmology).

in this series. In many cases, however, the color of the disk does not provide a sufficient basis for a diagnosis of atrophy. Its significance must be interpreted on the basis of visual function as brought out by visual field studies. Although the finding of definite atrophy is a confirmatory sign of visual loss and often indicates its duration, a lack of atrophy does not rule out chiasmal pressure, because severe visual field defects may be found before optic atrophy develops.

A loss of central visual acuity, as judged by a definite decrease or a reliable statement by the patient that his vision was definitely failing, was found in 32 per cent of the patients. Often, however, the patient continued to retain a visual acuity of 20/20 and was unaware of any visual disturbance, in spite of profound encroachment on the temporal fields.

Ophthalmologic changes of the remaining types were infrequent: diplopia resulting from extraocular muscle palsy occurred in only 5 per cent; pupillary changes other than those due to visual loss or ovular motor-nerve palsy in less than 1 per cent (1 case); possible involvement of the fifth cranial nerve in 1 case; papilledema in 4 cases (2.6 per cent), three of which were craniopharyngiomas and one an atypical chromophobe adenoma; and proptosis in only two.

Since optic atrophy and loss of central visual acuity are dependent on and demonstrated in the field defect, and since 96 per cent of the cases of pituitary tumor and craniopharyngioma show such a defect, the visual field examination is the most important single ophthalmologic criterion indicating the existence of such tumors.

Comment: This excellent paper reiterates in well-organized form the extreme importance of careful visual field examination in suspected pituitary lesions. Chamlin's techniques, described in previous articles (Arch. Ophth. 1950, *44:* 53; 1949, *42:* 126) are shown to good advantage. His equipment for testing minimal defects should be seen by all who have an opportunity to take his Academy course.

Although the authors state that the clinical signs in eosinophilic and basophilic adenoma are sufficient for diagnosis, it should be noted that cessation of menses in the female is often an important sign in chromophobe adenoma.

The percentage of hemanopic defects (96 per cent) in chromophobe adenomas certainly is higher than in other series, but I believe it reflects only the authors' skill in the discovery of minimal field changes.

The authors' reiteration of the lack of diagnostic aid of pallor of the disc should be pointed out. Pallor means nothing unless supported by visual field changes.

JOHN WOODWORTH HENDERSON

TUMORS OF THE OPTIC PAPILLA

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Am. J. Med. Sci., 1955, *230:* 213–225

Inasmuch as the optic papilla or optic disk is merely an intermediate segment of the visual nerve fibers, it rarely becomes the primary site of a pathologic process. Most of the changes found in it result from lesions in the tissues with which it is connected. Primary tumors, when they occur, not only require differentiation from inflammatory processes and congenital anomalies but must also be distinguished as benign or malignant, a distinction that can seldom be made on the basis of ophthalmoscopic appearances only. Ophthalmoscopic examination, however, may incidentally reveal the presence of a true primary tumor that has remained symptomless for some time. Although it may be doubted whether a glioma ever originates in the optic disk, gliomas of the intraorbital portion of the optic nerve may progress forward until they become visible with the ophthalmoscope. In some cases, the glial proliferation attains considerable size, forming a white or a cystic mass on the disk.

Meningiomas of the optic nerve sheaths may also invade the globe. In one illustrative case, histologic examination of an eye that had been blind for 20 years showed a fusiform tumor entirely surrounding the optic nerve immediately behind the globe and extending through the optic disk into the retina. The tumor, a dural endothelioma of the optic nerve, had compressed the nerve into a narrow, completely atrophic cord. About 10 per cent of the optic nerve tumors reported in the literature have been associated with von Recklinghausen's disease. The

stem cell in the tumors of this disease is the Schwann cell, which is not present in the optic nerve. Theoretically, therefore, the optic nerve should not participate in the manifestations of neurofibromatosis. Actually, however, the oligodendroglia cells in the optic nerve may perform the same function in that nerve that is performed by the Schwann cells in the peripheral nerves and so may be involved in the same process. If this reasoning is correct, the optic nerve tumor should be an oligodendroglioma; in most cases, however, gliomas of the optic nerve have been classified as astrocytomas.

Hyaline bodies in the optic disk are said by some authorities to be related to, if not identical with, the manifestations of tuberous sclerosis. Chambers and Walsh, however, who were unable to correlate them with any specific disease process in their patients, believe that they occur as a familial or hereditary anomaly in association with various conditions. Interestingly, hyaline bodies in the disks were found by them in only one of several hundred cases of verified intracranial tumor.

True angiomatous lesions of the optic nerve or optic disk are extremely rare and even those few that have been reported have been designated by various terms such as von Hippel's disease, endothelioma, cavernous angioma of the disk, venous angioma of the disk, angioma of the retina and hemangioma of the retina. Angiomatous lesions of the retina, sometimes connected by a tract of vascular tissue with a similar lesion in the midbrain, may be classified as racemose hemangiomas of the retina. The underlying defect in this syndrome is apparently a congenital vascular anomaly in which the retinal vessels are increased in number, size, and tortuosity; direct arteriovenous communications can usually be identified and small aneurysmal dilatations may be seen on the involved arteries.

Cysts of the optic disk may be either congenital or acquired. Those that are congenital are usually associated with other congenital anomalies, while those that are acquired are often found in patients with evidences of recent or old inflammatory processes in the deeper structures of the eye. Any blood vessels that may be present in the eyes with congenital cysts are empty, but those connected with an acquired cyst carry blood.

Carcinomatous metastases may invade the optic nerve or disk from primary tumors in distant sites, such as the stomach, the rectum, or the breast.

The question of origin arises especially in connection with melanomas, because the optic disk is generally regarded as a nonpigmented structure. Undoubtedly, juxtapapillary tumors have sometimes been incorrectly interpreted as tumors of the papilla. However, since the lamina cribrosa is potentially a pigment-bearing tissue, it would be possible for it to give rise to a malignant melanoma. Simple melanomas, presumably arising from uveal elements incorporated in the tissues of the disk, can not infrequently be seen as pigmentary plaques on the optic disk. Critical evaluation of 10 so-called primary melanotic tumors of the papilla showed that in most instances in which a malignant melanoma had its major localization in the optic disk, the growth was eccentric and involved tissues beyond the margins of the disk. Doubts have therefore been expressed whether

any of the cases reported as melanomas of the optic papilla have been proved indisputably to have originated in the papilla. Although the question of origin thus remains unsettled, it is certain that any pigmented mass on the disk should be closely observed and the eye removed if evidence of growth appears.

Comment: The author has covered this fascinating subject in his usual thorough and readable style. The recognition and classification of the tumors of the optic nerve head can give rise to real difficulty to the clinician who must accept responsibility for enucleation. In the first place, he must rule out certain congenital anomalies such as persistent Bergemeister's papilla tissue or massive medullation of the nerve fibers. When such anomalies are excluded the ophthalmoscopic picture fortunately need not be the sole criterion. Any patient with an unusual lesion of the optic papilla should be subjected to thorough ocular and general examination. The potential optic nerve gliomas should be checked for progressive exophthalmos, and the orbits and optic canals visualized by Roentgen ray studies. In a meningioma appearing at the disk, certainly involvement of the sphenoid wing should be ruled out. Other stigmata of von Recklinghausen's neurofibromatosis may be discovered—the café au lait spots for example. A good number of cases with neurofibromatosis will demonstrate small nodules in the iris by slit lamp microscopy. The characteristic field changes produced by hyaline bodies of the disk should be carefully mapped out. The neurologic changes of von Hippel-Lindau's disease should be looked for in any angiomatous lesion of the papilla. It is to be hoped that in most cases of metastatic neoplasm to the disk either the history of previous surgery or thorough physical examination would locate the primary lesion in many cases. It sould be remembered that a melanotic lesion of the optic disk in a Negro is less likely to be malignant than in the white races. The author's bibliography is recommended to those readers who are especially interested.

JOHN WOODWORTH HENDERSON

COMPLETE REMOVAL OF GLIOMAS AFFECTING THE OPTIC NERVE

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A. M. A. Arch. Ophth., 1955, *54:* 386–391

The prognosis in cases of glioma of the optic nerve depends upon the extent and the type of growth. A tumor involving the optic chiasm or the neighboring structures of the hypothalamus and third ventricle, or one which involves the optic chiasm and both nerves, offers a gloomy outlook both for the maintenance of vision and for the preservation of life over a long period. In those cases in

which the tumors are located primarily within the orbital part of the optic nerve, or with intracranial extension which is entirely prechiasmal, the prognosis is much more favorable.

The large majority of these tumors is of low malignancy and does not invade surrounding tissues and seems to extend centrally by propagation along the optic nerve. There are many reports in which long remission as well as apparent cure have occurred with mere biopsy of the lesion. However, because of the nature of the tumor it has been deemed wise by many to sacrifice the globe and even exenterate the orbit.

The neurosurgical transcranial approach to the orbit allows for visual microscopic identification and, in some cases, complete removal of the lesion with preservation of the eye which, although blind, may have satisfactory motion. Four patients with glioma of the optic nerve have been treated by the transcranial approach and resection of the involved nerve distal to the optic chiasm and proximal to the globe, thus removing the tumor and sparing the globe on the involved side.

The first case is that of a 3-year-old boy with left proptosis of three weeks duration and papilledema which was more marked on the left side than the right. Nothing abnormal was noted on the roentgenograms of the skull. The diagnosis of intraorbital tumor was made, and left transfrontal craniotomy allowed complete removal of an intracranial and intraorbital astrocytoma of the optic nerve. Twelve years later the patient was still in good health.

The second patient, aged 2 years, had a right divergent squint, paresis of the superior rectus muscle, right optic atrophy and loss of the direct pupillary reaction to light. Special views of the orbits did not show evidence of any abnormality. A fibrous astrocytoma located just anterior to the chiasm and immediately behind the globe was removed transcranially. Four months later there was ptosis, exophthalmos and partial immobility of the globe. Ophthalmoscopic examination showed an atrophic optic nerve with pigmentary changes about the disc margins characteristic of a nerve avulsion.

The third patient was 4½ years of age with right blindness, esotropia and slight proptosis. The pupil was fixed to light and the optic disc pale. A large dumb bell-shaped astrocytoma was removed transcranially and there was a satisfactory convalescence.

The fourth patient had a marked exophthalmos of one year's duration. The fundus showed wrinkling of the retina in regions above the macula. A right inferior altitudinal anopsia was present; the left was normal. An astrocytoma which extended both intra- and extracranially was completely removed through the transcranial approach. Nine years later there was no further change in the appearance of the eye. The right globe pulsated and was divergent.

The authors suggest that all patients suspected of harboring a tumor affecting the optic nerve be given the benefit of exploration with radical removal of the tumor when it is feasible. This yields a better cosmetic result than removal of the globe or orbital exenteration.

Comment: This excellent article points up the results which can be gained by full cooperation between neurosurgical and ophthalmologic consultants. Whether all such cases are primarily neurosurgical in approach is open to honest difference of opinion. If there is no evidence of intracranial extension clinically, a preliminary Kronlein operation with study of the cut end of the removed optic nerve will give a further indication for craniotomy. Although x-ray evidence of enlargement of the optic foramen is lacking in all four cases reported, this is still a good indication for craniotomy in a given case. The use of a plate over the orbital roof after the superior approach should be more frequent. Pulsating exophthalmos can occur when the orbital roof has been removed. I have seen one case of unilateral oscillopsia after removal of the posterior third of the orbital roof.

JOHN WOODWORTH HENDERSON

THE PUPIL

ON THE PUPILLARY CHANGE OF THE OPPOSITE EYE CAUSED BY THE STIMULATION OF THE OCULOMOTOR NERVE

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Yonago Acta Medica (Japan) 1955, *1:* 187–190

This study was directed toward analysis of the pupillary changes in the contralateral eye caused by stimulation of the homolateral oculomotor nerve. When the oculomotor nerve in cats was cut or stimulated mechanically or with a single electrical impulse the pupil of the opposite eye constricted. This constriction occurred after the removal of the brain cortex of the cerebral hemisphere on the side of stimulation. From this it is inferred that the pupillary constriction was caused by antidromic impulses stimulating the sphincter nuclei via a reciprocal communication between the two nuclei.

When the surface of the oculomotor nerve was stimulated by a faradic current the pupil of the opposite eye dilated during the stimulation and constricted after cessation of the stimulation. The pupillary dilation disappeared after tenotomy of the medial rectus or removal of the lateral rectus muscles. It is postulated that proprioceptive impulses are generated by extension of the lateral rectus muscle and that these impulses arrive at an unknown center in the homolateral brain cortex or subcortex. Then inhibitory impulses are discharged to the opposite sphincter nucleus via the caudal half of the corpus callosum and that there is pupillary dilation in the opposite eye.

Comment: This work is based on several assumptions which appear insufficiently proven:

(1) There is no satisfactory proof of a direct connection between the Westphal-Edinger nuclei of the right and left side. Experimental and clinical evidence rather point to the absence of such a connection. For example, when a lesion injures the posterior commissure and the pretectal area on one side, the light reflex is reduced or absent on the side of the pretectal lesion but not on the opposite side. Such findings would be impossible if the right and left constrictor nuclei were interconnected.

(2) The sixth nerve is a motor nerve which carries no known afferent fibers. In addition, no fibers are known to ascend from this motor nucleus to the cortex. Therefore, the reflex arc assumed by the author is highly questionable.

(3) In experiments performed in this laboratory, (cats and monkeys), intracranial stimulation of the third nerve did not cause movements of the contralateral eye and pupil, provided that (a) stray of current to the neighboring diencephalon and/or sensory 5th nerve fibers was avoided, and (b) the eye on the side of the stimulation remained closed. In the absence of this precaution the homolateral pupillary constriction and rotation of the globe can cause a change in the retinal illumination of that eye. This change affects the third nerve nuclei on both sides via the optic nerve, optic tracts, etc.

Finally, if the author's theory were based on facts, stretching of the external rectus muscle in anaesthetized cats would have to produce dilatation of the opposite pupil. This does not occur in cats or monkeys when the globe is rotated nasally as far as is possible (provided the rotated eye is shielded from light and the operation is done gently, to avoid sensory stimuli due to rough handling with sharp instruments.

OTTO LOWENSTEIN

THE ORBIT

PROPTOSIS IN INFANCY AND CHILDHOOD: A REPORT OF NINE CASES

R. HERTZBERG

Sidney, Australia

Trans. Ophth. Soc. Australia, 1954, *14:* 30–39

Proptosis in an infant may be due to the following causes (Duke-Elder, S., Textbook of Ophthalmology. Vol. V. London. Henry Kimpton, 1952):

1. Congenital deformities of the orbit diminishing its capacity.
   (a) Cranio-facial dysostosis.
   (b) Failure of development of the roof of the orbit following encroachment by orbital contents.
   (c) Orbital cephalocele.
   (d) Congenital cystic eyeball.
2. Orbital cysts or tumours.
   (a) Dermoids of the orbit and lacrimal region.
   (b) Teratomata.
   (c) Orbital tumours—endothelioma, fibroma, angioma, osteoma, sarcoma.
   (d) Orbital cysts developed as diverticula from the paranasal sinuses; cysts of the orbital lobe of the lacrimal gland.
3. Traumatic proptosis due to birth injuries, usually associated with fracture of the skull and retrobulbar hematoma.

The investigation of the cause of the exophthalmos should include a careful history, an analysis of the degree and the direction of the proptosis, an examination of ocular movements and fundi and palpation of the orbits. Roentgenograms of the optic foramina and sinuses should be made, together with serologic tests and blood studies.

Neuroblastoma of the adrenal gland is a tumor of childhood and very often discoloration of the lids and proptosis occurs before the primary tumor is evident. The average age of the patients is three years ten months and the younger the child the more rapid the course. A marked secondary anemia occurs constantly. Any child of less than five years having a proptosis and ecchymosis of the lids should be viewed as having a neuroblastoma.

Retrobulbar hemorrhage is often associated with trauma and with bruising of the lids. The absence of positive findings and the rapid disappearance of the proptosis usually indicates the diagnosis.

Proptosis may be due to an unknown cause and repeated investigations do not indicate the disease responsible. The author agrees with Reese (Tumors of the Eye, New York, Paul B. Hoeber Co., 1951) concerning the inadvisability of exploring an orbit without a palpable tumor:

"Unless a mass is palpable in the orbit no surgery should be attempted. I believe that no orbit should be explored, either for biopsy purposes or for excision of any possible lesion unless this lesion has manifested itself as a mass which can serve as an objective for the surgical approach. I cannot recall a single instance in which an orbit has been explored with benefit merely because there was an unexplained unilateral exophthalmos. In these cases temporizing is in order and an unabated effort should be made at regular intervals to determine the cause of the exophthalmos. The exception to this rule is the case in which some deep non-palpable orbital lesion is jeopardizing the function of the eye by pressure or by its effect on the optic nerve."

A hemangioma is characterized by rapid growth and a rapid onset. These tumors may remain dormant for years and suddenly become noticeable when thrombosis occurs. Surgical excision is probably the best treatment because the tumor is encapsulated and removal may be accomplished with little damage to surrounding tissue. If removal is incomplete, radium or deep roentgen ray therapy can still be given. The amount of radiation which may be required to destroy a large mass without resort to surgery would probably damage the eye and, in young people, also interfere with growth of facial bones.

Hydatid cyst of the orbit is uncommon and positive diagnosis is not always possible. Pressure symptoms occur early and these cysts appear more frequently in young adults. Complement fixation tests are frequently negative but an eosinophilia may add weight to the diagnosis. Roentgen ray studies following puncture of the cyst, withdrawal of fluid and injection of lipiodol may reveal a double-walled cyst.

Reactive edema of the orbit is the commonest cause of proptosis in childhood and is practically always due to infection in the paranasal sinuses. It may subside or be the prelude of a true orbital inflammation. Most cases of orbital cellulitis are reactive edema. The response to medical treatment is rapid and the temptation to make incisions into the lids should be resisted.

Metastatic abscess of the orbit occasionally arises in infectuous diseases, scarlet fever, chicken pox, influenza and from surgical operations for infection in other parts of the body.

Meningiomata in infancy are uncommon. The author reports the case of a newborn with a tumor weighing 240 gm. which was protruding from the orbit at birth. It was excised the following day and histologic studies indicated its origin from the meninges.

A meningioma may involve the orbit in any of three ways; primary in the sheath of Schwalbe; involvement of the sheath through the optic foramen; or involvement through invasion of the orbital wall. Opinion is divided as to the primary origin of meningioma within the orbit and if there is any evidence that the tumor is not confined to the orbital cavity craniotomy is mandatory.

Rhabdomyosarcoma of the orbit occurs predominantly in males at an average age of six to seven years. The treatment is immediate exenteration of the orbit.

Comment: In J. H. Doggart's "Diseases of Children's Eyes" (C. V. Mosby Company, 1947) several pages are devoted to the problem of unilateral proptosis among infants and children. Except for the generalities contained in this text and the occasional case report

of unusual or interesting conditions that might produce unilateral proptosis in this age group, the literature on this phase of orbital pathology is rather sparse.

The tissue comprising the orbital contents (eye excluded) in infants and children has the same potential for producing tumors and reacting to abnormal stimuli as does the orbital tissue of adults. Indeed, from a pathologic standpoint, almost every known neoplasm which might originate in the orbit has been reported to occur in both the young and old alike. However, from a clinical standpoint the disorders producing proptosis in infants and children usually are different from those in adults and the clinician is prone to consider a different group of disorders in his differential diagnosis than when dealing with a similar appearing proptosis in adults.

Therefore, it was refreshing to this editor to see an article, such as this, devoted to some of the orbital problems occurring in youngsters. It was disappointing, however, that the author could not have included a larger number of these interesting case studies and that the nine cases that were reported were not more representative of the common problems encountered.

Four of these conditions, (retrobulbar hemorrhage at birth, hydatid cyst of the orbit, metastatic orbital abscess, and meningeal sarcoma) would seldom be seen in the average clinical practice. The hydatid cyst, in particular is even more rare in the United States and Canada than in Australia. In the author's case the cyst ruptured at the time of its removal, but no adverse effects were noted because of the accidental release of the fluid contents. This is in contrast to other reports wherein the reader is warned of the severe toxic effects that followed the accidental rupture of the cyst.

The case described as a "meningeal sarcoma" is a very unusual one. The author points out that meningiomas are uncommon during infancy. In this particular instance a child was born with a very large (the gross specimen when removed weighed 240 grams and the diameter was 7½ centimeters) mass protruding from one orbit. The author's description of the histologic picture does not convince this reader that the growth was a true meningioma. On the basis of its large size and its presence at birth, the possibility of a teratoma should be considered.

Four (neuroblastoma, rhabdomyosarcoma, reactive edema, and hemangioma) of the author's case studies are rather representative of orbital conditions more commonly seen in children. The case studies of neuroblastoma and rhabdomyosarcoma are quite typical in that they point out the very rapid growth of these neoplasms, their resistance to therapy, and the fatal prognosis so common in the majority of sarcomas of the orbit in childhood.

The author uses the term "reactive edema" much as does Duke-Elder to indicate a reaction of the soft tissues of the orbit secondary to or as an accompaniment of some inflammatory process, such as sinusitis, in an area adjacent to the orbit. In the North American continent the term orbital cellulitis is more loosely applied to this situation. The author correctly warns the surgical incisions or surgical interference are strictly contraindicated in this situation and that with conservative care, over a period of several days to several weeks, the inflammatory process will subside. The editor would also like to point out that deep x-ray therapy given through a lateral portal is also of great help in assuring complete resolution of these inflammatory conditions. The author feels that the cases of reactive edema are the commonest causes of unilateral proptosis in childhood. In the editor's experience the incidence of this type of orbital disease has shown a marked drop in the past ten years; the decrease being attributed to the more frequent and quicker use of antibiotics in cases of upper respiratory disease in children. In the editor's experience cases of reactive edema are less commonly seen than are orbital neoplasms and congenital anomalies.

The case described as "hemangioma" proved to be one of the cavernous type. The editor agrees with the author that this type of hemangioma should be removed surgically rather than treated with radium, x-ray, or sclerosing solutions. It should be emphasized that this statement applies to those hemangiomas situated in the orbit and accompanied by proptosis but does not apply to hemangiomas of the eyelids.

In the case of "unilateral proptosis of unknown origin", the child was observed for two years. The author refrained from advising exploration of the orbit because of the absence of a palpable mass and the retention of good vision. The author has precedence for this approach in a dictum expressed by Reese "Tumors of the Eye" (Paul Hoeber Company, 1951). It was Reese's feeling that no orbital surgery should be undertaken in the absence of "a mass which can serve as an objective for the surgical approach" unless an unknown lesion in the deep orbit is jeopardizing the function of the optic nerve. Reese's dictum is a very good one and should serve as a warning to those ophthalmologists (of which there are many) who are anxious to "take a piece or sample" from the orbit but are quite unfamiliar with the surgical anatomy and operative hazards in the posterior orbit. In the author's case, however, it is believed that he took Reese's advice much the literally in allowing the child to go two years without removing the mischief. In the editor's opinion there is a very good chance that a slow growing neoplasm such as an astrocytoma might be present in this situation. The slow growth of such a neoplasm may fill up every nook and cranny in the posterior orbit before affecting vision; a course quite in contrast to the usual tumors of childhood in this locality. An orbitotomy either through a lateral approach or a transfrontal approach might have been done on this case when the proptosis did not show signs of receding after an observation period of six months.

JOHN W. HENDERSON

THE RETINA AND VITREOUS

PRECIPITATES ON THE VITREOUS

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Ophthalmologica, 1955, *130:* 191–200

Precipitates, consisting of accumulated cellular deposits, may appear in any part of the eye where there is a fluid-containing cavity or where such a cavity has been produced by some inflammatory process. An interesting example of this phenomenon came under the author's observation in February, 1953, when a 26-year-old man was admitted to the hospital because of pain and a slight reduction of visual acuity in his right eye that had first been noticed by him four weeks before. Examination of the right fundus showed a focus of active chorioiditis in the nasal superior quadrant about four disk diameters in size. The sclera was visible at the peripheral border, bounded by a hazy, narrow pigmentary zone. The rest of the focus was covered by a dense opacity of the vitreous, which contained many corpuscular elements, mostly posterior. Macular edema and papilledema were also present. No signs of illness were found on general examination. Treatment consisted of bed-rest, local application of atropine, and systemically 3 gm. of salicylates daily, but in spite of this the inflammation increased in intensity and the macular edema extended until it reached the chorioretinal focus. Simultaneously, detachment of the vitreous, which was turbid because of the many cells it contained, was noted over the central part of the retina and the hyaloid membrane in the detached region was seen to be thickened. Within the next few days, many grayish-white spots developed on the posterior surface of this membrane where they remained without change until June. Slow healing of the inflammatory process took place during the months that followed, and at the same time the spots on the vitreous became more translucent and then decreased in size and number, until at last they disappeared completely. No changes, other than the cells in the vitreous, were seen in the anterior segment of the eye at any time during the course of the disease.

In all probability, structural changes decreasing the permeability of the hyaloid membrane provide at least a partial explanation for the fact that certain cells remained on its surface, mostly in flat conglomerates, while others invaded the vitreous and remained isolated therein. Little gray infiltrates originating from the perivascular foci in a patient with a tuberculous periphlebitis near the papilla have been seen to migrate freely into the vitreous by way of an annular hole in the hyaloid membrane in front of the papilla. Such a hole, however, could not be observed in the patient here reported, and its absence, too, was probably partly responsible for the unusual localization of the precipitates. In addition, it may be noted that the little gray infiltrates referred to were clearly different from the flatter, patchy ones found in the present case.

Comment: The author's conclusion that the detached hyaloid membrane upon which the striking, clinically visible precipitates were visualized, had become altered and densified, and thus less permeable, is quite credible.

Clinical observation could not take him further. In this connection, cellular growth on the posterior surface of the detached vitreous, not only in old cases of vitreous detachment, but in relatively recent ones (Klien, B. Amer. J. of Ophth., 1955, *40:* 515) is of special interest. Wandering cells produced by a post-traumatic or by an endogenous inflammation and cast off upon the posterior surface of the detached vitreous become fibroblast like and very elongated, often joining up with one another. In this way, although histologically inconspicuous, a membrane may form on the posterior vitreous rendering this surface tougher and less permeable.

BERTHA A. KLIEN

CONTRIBUTION TO REACTION OF RETINAL VESSELS IN UVEITIS

W. FRIEMANN

Klin. Monatsb. f. Augenh. 1955, *126:* 129–133

Kyrieleis in 1933, described changes in the fundi of patients with uveitis which he considered to be manifestations of atypical tuberculosis, and for which he proposed the term periarteritis nodosa tuberculosa retinae. Friemann describes a similar case in a 21 year old man in whom the uveitis was associated with the appearance of circumscribed white spots on the wall of the lower temporal retinal artery. Two additional cases of uveitis are described. The first in a 26 year old man in whom the uveitis was associated with circular, not sharply demarcated, gray foci and partial constriction of the lumen of all the larger veins of the retina. The second occurred in a 15 year old girl, in whom numerous whitish, not sharply defined spots were observed on the veins of the retina. One is tempted to assume a special disease entity since in some cases the associated reactions were limited to the arteries of the retina, while in other cases they were limited to the veins. The author, however, believes that the changes described in these patients may be considered to be an extreme reaction of the retina associated with the uveitis. Less pronounced forms of an associated reaction of both portions of the retinal vascular system, i.e., isolated, more or less temporary, infiltrations of the walls of the retinal vessels may occur quite frequently in uveitis. It seems noteworthy that the course of the uveitis was more acute in the patient with changes in the retinal arteries and that the uveitis was somewhat lingering in the patients with changes in the retinal veins.

Comment: Observation of secondary changes in the retina in anterior or posterior uveitis could be of aid in the prognosis of a given case if larger groups of patients were studied with the care to detail shown in this and other current publications (see also

Van Den Heuvel, Ophthalmologica 1955, *130:* 191, abstracted above) and if in this way a common denominator could be demonstrated for certain groups.

There is, for instance, the mild lymphocytic infiltration and edema of the retina in "retinitis serosa" (Samuels, B., Amer. J. Ophth. 1936, *19:* 493) associated with chronic post-traumatic infiltrating iridocyclitis after surgical procedures or injuries. There is, perhaps more often than might be suspected, a central angiospastic retinopathy from toxic or bacterial allergic influences upon the perimacular arterioles and pre-capillaries concurrent with or preceding the outbreak of a uveal focus of inflammation (Klien, B. Amer. J. Ophth. 1953, *36:* 1). There are preretinal precipitates and precipitates on the posterior surface of a detached vitreous in addition to the periphlebitis and periarteriolitis described by the authors (see also, Muncaster and Allen, Arch. of Ophth. 1939, *21:* 509). None of these findings are too obvious, but if looked for, may be found with the modern slit-lamp attachments.

BERTHA A. KLEIN

OSLER'S ENDOCARDITIS AND LESIONS OF THE FUNDUS

B. AUVERT AND M. A. VERGEZ

Bull. Soc. d'Cphth. de France, 1955, *7:* 458–460

An interesting example of the coexistence of two separate conditions, both of which are accompanied by ophthalmologic lesions, was presented by a 28-year-old man admitted to the Hôpital Lariboisière in December, 1954. He had had repeated attacks of acute rheumatic fever since he was 14 years old, and during the nine months preceding his admission they had followed one another practically without intermission. His temperature was 38 C.; he was very weak and extremely pale, and his spleen was enlarged. Signs of mitral disease were evident on examination of his heart, and blood cultures showed a nonhemolytic streptococcus. The diagnosis of subacute bacterial endocarditis superimposed on rheumatic heart disease was obvious, but two points of interest attracted attention: an abnormal blood picture and lesions in the fundus of the eye. The hematologic studies showed anemia (1,600,000 red blood cells), accompanied by a leukocytosis (20,000 white blood cells); the myelogram was normal. Eye-ground examination revealed the presence of extensive lesions, consisting of a milky white edema, vascular dilatation, hemorrhages, and exudates, affecting both eyes symmetrically. In spite of their intensity, however, the patient made no complaint of ocular functional disturbance. Tests for visual acuity could not be made because of his poor condition. No changes in the appearance of the fundus were noted during the remainder of his illness, which was brief because in less than 10 days he died in a state of collapse.

Anemia occurs frequently in Osler's subacute bacterial endocarditis, sometimes even dominating the clinical picture and leading to an erroneous diagnosis of

pernicious anemia. Lesions of the fundus accompanying endocarditis have often been reported, with some authorities considering Roth's white spots and hemorrhages and exudates to be pathognomonic of this condition. The authors, however, believe that the only ophthalmoscopic picture that should be considered characteristic of subacute bacterial endocarditis is the one presented by obliteration of the central retinal artery at the level of its trunk or in one of its branches. This obliteration results from a thrombosing arteriolar endothelitis that is a distinctive element in subacute bacterial endocarditis. On the other hand, lesions of the fundus such as those seen in this patient (vascular dilatation, hemorrhages, and exudates) are not produced by the same mechanism and are not characteristic of the disease. In this case, they were apparently due to the patient's severe anemia. Anemia of any kind, in fact, if sufficiently severe and prolonged, may cause hemorrhages and exudates by producing changes in the walls of the retinal vessels which permit the transudation of blood or plasma.

The findings in this case suggest that when subacute bacterial endocarditis is accompanied by retinal hemorrhages and exudates, it probably represents a severe, anemic form of the disease for which the prognosis should be guarded. Fortunately, because of earlier diagnosis and more active treatment, such forms are rarely seen to-day.

Comment: This case illustrates well the importance of analyzing lesions in the fundus which develop in the course of a retinopathy. It is not sufficient to state the presence of "exudates" and hemorrhages. Whitish retinal lesions may be of greater or lesser diagnostic and prognostic importance. It is usually possible to distinguish between those indicating chronic anoxia of the retina, such as lipoid deposits, and old inspissated exudates from those pointing to the more acute processes of arteriolar or capillary occlusions (cotton-wool areas), or those caused by toxic damage to the vascular endothelium in septic diseases (Roth's spots), of which the above case is an example.

In this way, the occasional co-existence of two independent pathological conditions, as the septic endocarditis and the severe anemia in the author's case, may be suspected early and in time to direct specific therapy from our ever increasing armamentarium toward each of these.

BERTHA A. KLIEN

CENTRAL SEROUS RETINOPATHY

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Brit. J. Ophth., 1955, *39:* 605–618

Central serous retinopathy has been described under many other synonymous terms, all of which, with the possible exception of disciform degeneration of the

macula, should now be swept away. It occurs typically in active, intelligent men ranging in age from 20 to 45 years. Earlier, transient attacks of blindness are occasionally reported. Defective or distorted central vision appears either suddenly or indeterminately in one or, more rarely, in both eyes. The onset, however, is not usually simultaneous in both eyes when both are affected. Metamorphosia can always be elicited and has therefore been used as a diagnostic test for macular edema. Ophthalmoscopy reveals a dark-reddish appearance of the macula with loss of the normal reflexes and often some retinal elevation. Fine punctate hemorrhages and yellowish-white spots may be observed; the vessels are usually normal, but occasionally constrictions and contiguous hemorrhages or infiltrations may be seen. The rate of appearance and progression of these changes varies widely from case to case. Resolution may ultimately be complete, though the "edema" persists for 6 or more months, or a residuum of fine pigmented or atrophic areas, or other abnormalities, may remain indefinitely. The elevation, in certain cases, may fail to subside and may even enlarge further, becoming paler as the overlying tissues atrophy, producing a variety of the condition known as "juvenile" disciform degeneration of the macula.

The cause of the disease is not known with certainty; bacterial infection, allergy, and toxic processes are favored by some authorities, while others hold a primarily functional neurovascular lesion responsible. It is quite likely that certain persons are, for one reason or another, peculiarly susceptible to an attack, but an immediate essential cause, possibly infective, should not be ruled out. The clinical picture, and the few eyes that have come to the pathologist, indicate a nonspecific lesion, initially functional and exudative with possible vasospasm and hemorrhages, followed by varying degrees of absorption and resolution, rarely with a mild degree of organization. Elsewhere in the body such a lesion would probably pass unnoticed, but the retina, with its considerable energy requirements and neural nature, responds badly to any trauma. The exact location of the lesion is in some doubt; it is probable that both retina and choroid are involved in most cases.

Treatment may vary from the use of vasodilators, diuretics, and sedatives, and even psychoanalysis, to the mass elimination of septic foci and antibiotic therapy. The true value of these, and of cortisone, which theoretically should be efficacious, is hard to assess, because of the rarity of the condition in the experience of most authors, and its frequently noted tendency toward full spontaneous recovery.

The typical clinical picture of central serous retinopathy was presented by 22 patients observed by the author; five others differed only in showing permanent and to some extent progressive retinal elevation with an excess of degenerative changes. These two groups have been considered separately in some respects, although many investigators claim no essential difference in cause, the basic lesion in disciform degeneration of the macula being a rupture of Bruch's membrane with transudation of plasma or blood. Analysis of the findings showed that a fair number of the patients suffered from the so-called "stress diseases," including peptic ulcer and migraine, and that some had multiple afflictions. Only

four possessed what could be called septic foci. All but five either gave a history of undue worry or overwork over a protracted period, or had an inadequate, obsessional, tense type of personality. In general, patients with central serous retinopathy are apt to be engaged in work requiring high-grade vision; but whether the condition has a predilection for persons engaged in such work or whether these persons are the ones most likely to notice an attack and seek advice, especially when the condition is unilateral, is not clear. The duration of the attacks was found to increase (but not significantly) with age; visual prognosis, however, deteriorates significantly as age rises and is distinctly bad in disciform degeneration.

Comment: Despite the fact that the author is a victim of the confusing terminology applied to the functional disturbances of the macular region, which he himself deplores, his paper is interesting because of the painstaking analysis from all possible angles of his series of 27 patients.

It is, however, not broadening our views of these disturbances as much as it could have done, and as much as the author apparently had intended for it to do, had he not included cases of disciform macular degeneration (Khunt-Junius).

PERSISTENT HYPERPLASTIC PRIMARY VITREOUS: THE JACKSON MEMORIAL LECTURE

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Am. J. Ophthal., 1955, *40:* 317–331

Persistent hyperplastic primary vitreous and persistent hyperplastic vitreous are the terms used to designate the condition often called "persistent tunica vasculosa lentis" or "persistent posterior fetal fibrovascular sheath of the lens." The tunica vasculosa lentis is actually a very meager layer of small vascular channels surrounding the lens and stemming from three sources: the hyaloid artery, the vasa hyaloidea propria (these are derived from the vessels which pass into the peripheral parts of the vitreous and enter the vascular tunic of the lens at its equator), and the anterior ciliary vessels which stem from the major arterial circle of the iris.

The anterior part of this vascular tunic of the lens is supplied by the ciliary system and normally shows a complete regression at about the eighth month of fetal life. The posterior part is fed by the hyaloid system and usually shows complete regression at about the seventh fetal month. Clinically the two portions seem to have little or no relationship, persistence and hyperplasia of one occurring independently of the other.

Eyes with persistent hyperplastic vitreous are often removed either with a diagnosis of retinoblastoma or because of the development of complications leading to enucleation. Pathologically the fibrous tissue back of the lens varies a great deal in extent and thickness. There are various degrees of vascularization and fat, smooth muscle, calcium deposits, cartilage and undifferentiated neuroepithelium may be present. The lens is smaller than normal and the ciliary processes are elongated. The retina appears normal and capable of good function.

In 90 per cent of the cases the lesion is unilateral with a perfectly normal fellow eye. The affected eye has a shallow anterior chamber and is almost invariably smaller than its fellow. The tissue back of the lens is usually densest in the center and has a pinkish white color which varies in size from a small plaque to an area completely covering the posterior surface of the lens. There is always some vascularity of this tissue, and vessels frequently radiate from the center. When the pupil is dilated, the ciliary processes can be seen extending toward, into or anterior to the periphery of the opaque tissue. These long ciliary processes are a characteristic feature of the disease and often serve as a differentiating point in the diagnosis. The lens is at first clear and later becomes cataractous with the first changes seen at the posterior pole. Swelling of the lens may cause a secondary glaucoma.

Retinoblastoma is the condition most frequently confused with persistent hyperplastic vitreous. It may be differentiated by the microphthalmia, the shallow anterior chamber, the long ciliary processes, the development of cataract and the opaque tissue against the lens in hyperplastic vitreous.

Early uncomplicated cases may be treated by removal of the lens by one or more needling operations and then by a discission through the fibrovascular tissue. In cases in which there has been spontaneous absorption of the lens and only retrolental tissue remains, a discission of the membrane may be performed. In cases which have shown evidence of deep spontaneous hemorrhage, treatment has been unsuccessful. In untreated cases ending in glaucoma, cyclodiathermy may be indicated or enucleation.

Comment: Dr. Reese's study shows that a carefully taken history and a painstaking examination of eyes with congenital opacities in or behind the lens, associated with perhaps other slight malformations of the anterior segment, may be quite rewarding. Many of these eyes are removed eventually because of later complications which could have been prevented by timely surgery. Histologically, the posterior segment often proves to be normally developed and shows only signs of the secondary complications.

The fact that these eyes with hyperplastic vitreous are most often misdiagnosed as congenital cataracts is not too disastrous since the first surgical step in hyperplastic vitreous is removal of the lens by discission. Discission of the lens alone will, however, not result in the desired pupillary opening. The practical point here is that the surgeon be familiar with the idea of a possible hyperplastic persistent primary vitreous behind what appears to be only a secondary membrane. With this possibility in mind, he will choose an exquisitely sharp knife and, by a well centered vertical incision into the membrane, will avoid injury to the hyaloid artery.

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The author divides his 27 cases into two groups, one comprising 22 cases with the typical picture of the purely retinal form of the functional disease, the other comprising the remaining 5 cases, which are apparently a mixture of true disciform macular degeneration and of the combined, chorioretinal form of the functional disease. The latter often takes a more destructive course and leaves a clinical and histological residual picture which greatly resembles that of the true disciform degeneration and thus gave rise to the confusing term of "juvenile disciform degeneration".

The author appropriately suggests that the synonyms for the group of apparently functional lesions be "swept away" in favor of a single term. He chooses "serous retinopathy".

The unity of this group should, however, not be disturbed by separating the cases with a milder course (purely retinal) and those with a more severe course (participation of the choroid in this process). If the term "serous retinopathy" is preferred to that of "angiospastic retinopathy", similar terms of "serous chorioretinopathy" and "serous choriopathy" may be used for the combined and more destructive processes.

The differential diagnosis between the residua of the chorioretinal or the choroidal form of the functional disease when accompanied by deep hemorrhage, and a true disciform degeneration of the macula, may indeed be quite difficult at first, or even impossible in the rarer instances when the functional disease occurs bilaterally and in an older individual. Principally, however, the distinction between the two should be upheld for therapeutic and prognostic purposes. There is no known therapy for the disciform degeneration, which seems to be truly a degenerative process centering around Bruch's membrane, and which, furthermore, is invariably bilateral, even if the involvement of the two eyes may be separated by many years.

In the functional disease therapy should always be attempted and it takes evaluation of the individual case to choose between antispasmodics, cortisone, antibiotics (in the presence of septic foci) and psychotherapy.

BERTHA A. KLIEN

HEREDITARY DISEASE

ADVISING PATIENTS WITH HEREDITARY EYE DISEASE

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Am. J. Ophth., 1955, *40:* 412–417

Many of the hereditary features connected with the eyes are of academic interest only, but others represent serious familial conditions which are particularly important to understand. Mere recognition of a hereditary disease is not enough. The physician should be able to diagnose the type of inheritance and make predictions for the patient's offspring, as well as for other members of his family. Abnormal genes affecting the eye make their presence known by producing either dominant, recessive, or sex-linked recessive traits. Traits that appear freely in both men and women alike, without regard to sex, are often referred to as autosomal. Every abnormality must begin somewhere, and patients may be seen with a disease which they are going to transmit to many future generations, although their own family history is completely normal. Such patients are mutants, and the defective gene first appears in them.

Dominant traits are always obvious. That is, if an individual carries the gene for a simple dominant feature, then he must show the feature whatever it is. If a particular disease is inherited as a dominant trait, it may be expected to appear in approximately 50% of the members in each generation of the affected family. Predictions can therefore be made with reasonable accuracy concerning the offspring and relatives of a patient with an eye disease that is inherited as a dominant trait (tables 1 and 2). If the patient is young, his parents may wish to know the likelihood of this disease appearing in subsequent children. They can be told that the next child will have a 50 per cent chance of presenting the disease. As for the patient himself, if he marries a normal person, one-half of his children will be affected. The normal members of the family, such as his brothers, sisters, aunts, and uncles, cannot be carrying the dominant gene and need not fear the possibility of having affected children. Only in irregular circumstances can anyone transmit a dominant gene without himself giving evidence that it is contained in his own germ plasm.

Irregular dominance is found when a patient, whose eyes are apparently normal, transmits a disease such as glaucoma. This phenomenon may represent an effect of environment upon heredity, as in the case of a patient who has lived a protected life free from emotional trauma and whose eyes are therefore normal although he has a tendency toward glaucoma. Apparently normal members of a family with hereditary glaucoma should always be carefully followed, because

TABLE 1

How to Determine the Mode of Inheritance

DOMINANT
1. One of the parents is affected
2. Fifty percent of the members are affected
3. Normal members have all normal children

RECESSIVE
1. Neither parent is affected
2. The parents are usually related (consanguineous union)
3. Twenty-five per cent of the siblings are affected
4. Affected members have normal children*
5. Normal members have normal children*

SEX-LINKED RECESSIVE
1. Affects only men
2. Transmitted via the normal women
3. Affected men have normal children*
4. Normal women have 25 per cent of their children affected (i.e., 50 per cent of the males, no females)

* Normal here means the phenotype. The individual may still be a carrier but will not have the disease.

TABLE 2

What Are the Chances My Next Child Will Develop the Disease?

Type of Heredity	Person Asking Question			
	Parents of the patient	The patient	Normal aunts & uncles	Affected aunts & uncles
Dominant	50%	50%	0	50%
Recessive	25%	0	0	0
Sex-linked recessive	(50% of sons) (none of daughters) 25%	0	Women 25% or less men 0	Affected uncles may transmit but will have normal children

the disease may appear at some later date, even though provocative tests have been initially negative.

Retinoblastoma is a dominant trait, and if it appears in a child whose parents have perfectly normal eyes, it can be assumed to be the result of a mutation. The chances, in this case, that another child of the same parents will have the defect, are only about one in a hundred. Patients with retinoblastoma, however, if they survive, should be advised not to have children, since they are certain to transmit the disease to 50 per cent or more of their offspring.

Cataracts sometimes show a dominant hereditary tendency, but in most cases their occurrence is sporadic.

The advice given to patients with a recessive disease should differ considerably from that given to patients with a dominant one. Even though both parents may carry a recessive trait, the chances are only one in four that their next child will manifest the disease. As for the patient himself, if his mate is normal,

he will not transmit the abnormality to any of his children. All of them must be normal. A defective gene must come from each parent before the disease will be apparent.

Sex-linked traits are peculiar in one respect, from the standpoint of ophthalmology. They are transmitted by both sexes, but they affect only males. Parents with sex-linked traits should be informed that half their sons may show the disease, but their daughters never will, although they may be carriers. The patient himself, being an affected male, will never have any children with the disease, although here again his daughters may be carriers.

Certain other important eye conditions may be transmitted by any one of these three methods. Two or three generations must therefore be plotted before the type of inheritance in a particular case can be determined and suitable advice given. Moreover, since nearly all important eye diseases may appear sporadically, without any hereditary features, the hereditary character of the condition, as shown by its presence in preceding generations, must always be determined before any predictions are made, concerning its probable occurrence in the future.

Comment: Dr. Manchester presents, in easily understandable terminology, a cautious and valuable addition to the growing literature designed to stimulate, in the ophthalmologist, an awareness of the role of the gene in the determination of ocular disease. Mendelian principles are explained and then applied to the problem of advising a genetic prognosis in certain types of inheritance patterns. All prognoses, of course, must depend upon the affected individual's specific pedigree. This necessitates a knowledge, on the part of the physician, of Mendelian principles in addition to knowing how to take a pedigree and to interpret it.

Prognostic pitfalls encountered in dominant inheritance patterns are: (1) late onset of the disease in an individual, (2) mutation, and (3) irregular dominance. Each factor requires and depends for its recognition upon a meticulous personal study of the particular family by the interested physician. The author's statement that the same clinical entity may be transmitted by different inheritance patterns in certain families must be reemphasized. It is most important that each family, via its own particular pedigree, be carefully analyzed before one is capable of the giving of a genetic prognosis.

HAROLD F. FALLS

OPTHALMOLOGIC OBSERVATIONS CONCERNING THE SYMPTOM COMPLEX OF STURGE-WEBER'S DISEASE, KLIPPEL-TRÉNAUNAY AND PARKS-WEBER SYNDROMES

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Klin. Monatsb. f. Augenh., 1955, *126:* 154–164

The term Sturge-Weber disease was coined in 1936 for a disease characterized by the triad of unilateral vascular nevi of the skin and particularly of the face, congenital or acquired glaucoma and angiomatous changes of the pia mater. The changes in the pia mater are congenital malformations of the cerebral vessels, but congenital malformations or neoplasms also have been observed in other organs such as the retina, the lung and the colon. The disease is essentially one of dilatation of the vessels in ectodermal organs. Abnormalities of the vascular apparatus are also present in the syndromes described by Klippel-Trénaunay in 1900 and by Parks-Weber in 1907 for which the terms "nevus varicosus osteohypertrophicus" and "hemangiectasia hypertsophicans", respectively, were coined. The fact that the symptoms of those three conditions may overlap or may combine suggests a close nosologic and pathogenic relationship.

A mixed case is described in a 4-year old boy with bilateral pronounced vascular nevi of the skin, definite capillarectasia on the soft and hard palate, and bilateral buphthalmos. These manifestations are classic characteristics of Sturge-Weber's disease. The flat vascular nevus and the osteohypertrophy of the right facial portion of the patient's skull and of the right leg were symptoms which occur in Klippel-Trénaunay and Parks-Weber syndromes. Since buphthalmos, besides the vascular nevus, is frequently the first apparent symptom, an ophthalmologist may be initially consulted. Thus, it may be his task to investigate the clinical aspect and to determine the course of the treatment, which occasionally may extend over several years, in as much as additional symptoms may develop later. The ophthalmologist, therefore, can contribute to the final clarification of the diagnosis.

Comment: The point, stressed by the author, namely that the ophthalmologist who possesses knowledge of the range of symptomatology and signs exhibited by the neurocutaneous syndromes is in an excellent position to be of service, diagnostically, to his colleagues in other medical disciplines is worthy of re-emphasis. These syndromes, including Sturge-Weber, neurofibromatosis, angiomatosis retinae and epiloia, are hereditary, exhibit a rather marked protean symptomatology varying in degree and intensity, usually present congenital evidence of their presence (phako-spot) and manifest neo-plasia which dwell in the twilight zone between benign and malignant states. The ophthalmologist who possesses a knowledge of the wide range of symptomatology of Sturge-Weber syndrome and who is aware of the hereditary nature (irregular dominant pattern) of the entity is in an excellent position to be of service to his medical colleagues, the patient, the patient's family and even to unborn generations.

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MANDIBULO-FACIAL DYSOSTOSIS (TREACHER COLLINS SYNDROME)

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Arch. Dis. Childhood, 1955, *30:* 391–395

In the light of evidence obtained from careful dissections of the facial region in an infant with a typical case of mandibulo-facial dysostosis (Treacher Collins syndrome), the authors advance the suggestion that the original lesion in this syndrome lies with the stapedial artery.

The patient was admitted to the Royal Aberdeen Hospital for Sick Children at the age of 2 weeks because he failed to feed easily. He was born at full term of healthy parents; his birth weight was 5 lb. 11 oz., and he breathed well after birth. A three year old brother was alive and well. No history of any abnormality suggestive of dysostosis was elicited. On admission he was described as "a bird-like creature with rather curious eyes and a receding chin." In spite of continued attempts to feed him the right quantity of calories, he failed to gain weight. He had occasional cyanotic attacks and, finally, at the age of 10 weeks, he died.

On dissection, similar abnormalities were found on both sides. Analysis of the arterial abnormalities led to the conclusion that a defect of the stapedial artery causes maldevelopment not only in its own area of distribution but also in the region of the first visceral arch, whose vessels the stapedial artery normally supports during the critical phase between the disappearance of the first aortic arch and the full development of the external carotid artery, just after the formation of the primitive face. The inception of the abnormality can thus be placed in the sixth week of intrauterine life. All recorded abnormalities constituting the Treacher Collins syndrome, however severe or variable they may be, can be accounted for under this theory. The fact, that the defects of bones and soft tissues are confined to the face, can similarly be explained by the possibility of a normal stapedial capable of supplying the posterior end of the second visceral arch and no more. Present opinions concerning the normal development of the arteries in and near the first visceral arch should be modified in accordance with the anatomical findings in this case.

Comment: The authors' refinement of the previously held and less critical theory as to the causation of *mandibulo-facial dysostosis*, namely anomalous development of branchial clefts, is indeed intriguing. McKenzie and Craig intimate that all the known variations of this syndrome may result as a consequence of aberration in development of the stapedial artery. This concept, however, may be somewhat difficult to apply to such frequently encountered associations as: (1) anomalies of the calvarium, (2) anomalies of the cervical vertebrae and (3) stature aberration (dwarfism). The burden of proof is upon the shoulders of the author and future investigators. Arteriography might well be employed profitably in all such future investigations.

HAROLD F. FALLS

SYSTEMIC DISEASE

CONJUNCTIVAL BIOPSY IN SARCOIDOSIS

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Brit. M. J., 1955, 1180–1181

Although previously considered uncommon, conjunctival sarcoidosis has been so often found in patients with generalized sarcoidosis that conjunctival biopsy appears to have diagnostic value, even when there are no ocular symptoms. The sarcoid lesion occurs in follicles which are just visible to the naked eye and are best seen with the slit lamp. They are small elevations which are translucent and slightly yellow in color. Follicles are usually found in the fornices but may be encountered in the bulbar conjunctiva, sometimes as part of a sclerokeratitis.

Biopsy material is obtained following the local instillation of four per cent cocaine into the eye. A small fold of fornix conjunctiva about two mm. long containing follicles is grasped with forceps and snipped off with one cut of the scissors. A suture is unnecessary and there is little bleeding. The specimen is fixed in formol-saline and 50 serial sections are cut and examined.

Interpretation of the histology is more difficult than in liver or lymph nodes owing to the normal presence beneath the conjunctival mucous membrane of chronic inflammatory cells and lymphoid tissue. For this reason serial sections are essential, together with familiarity with the histology of sarcoidosis elsewhere.

Twenty-eight conjunctival biopsies have been done. Ten were on material from patients with generalized sarcoidosis without ocular symptoms. Sarcoid lesions were found in three; one of these had histologic confirmation by a liver biopsy and another showed typical sarcoid lesions in the conjunctiva even though a previous liver biopsy had not done so. Eighteen were patients who presented with uveitis or episcleritis of a type which suggested the possibility of sarcoidosis. Six of these were found to have generalized sarcoidosis, and four of the six had a positive conjunctival biopsy. The remaining 12 had no signs of systemic sarcoidosis, but in three of these typical sarcoid lesions were found at the biopsy. Thus in 16 patients with the generalized disease a positive conjunctival biopsy was obtained in seven.

Comment: In generalized sarcoidosis ocular involvement is very common. Woods (1951) reported granulomatous disease of the eyes in 44 per cent of such cases, an incidence only exceeded by involvement of the lungs (83 per cent) and lymph nodes (73 per cent). However, clinical involvement of the conjunctiva in sarcoidosis has been considered to be quite rare. The ocular findings are helpful in suggesting the diagnosis of systemic sarcoidosis, but definitive diagnosis depends upon histologic proof, usually biopsy of a lymph node.

In this very provocative paper, the authors suggest the more frequent use of biopsy of conjunctival follicles to establish a definitive, histologic diagnosis of sarcoid. The biopsy

procedure is remarkably simple and without complication. It is best to select the site of biopsy carefully by slit-lamp observation. The finding of a positive conjunctival biopsy in seven of sixteen patients with generalized sarcoidosis suggests that conjunctival involvement is much more frequent in this disease process than has been previously suspected. The procedure of conjunctival biopsy deserves more extensive use and further study. It should prove of great help in establishing the etiologic basis of some cases of granulomatous uveitis, as well as assisting the internist in the differential diagnosis of disseminated sarcoidosis.

BERNARD BECKER

PRESENT-DAY CONCEPT OF DIABETIC RETINOPATHY

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Diabetes, 1955, *4:* 284–289

The characteristic vascular lesion of diabetic retinopathy consists of great numbers of minute saccular aneurysms in the retinal capillaries. Often the aneurysms are hyalinized. Two possible explanations for the formation of these aneurysms are increased capillary pressure and histochemical changes favoring their development. Study of histologic specimens in which localized retinal venous occlusions were associated with an abundance of newly formed capillary collaterals showed that these newly formed vessels were free from aneurysms. Increased capillary pressure in itself, therefore, does not seem to be sufficient to cause the aneurysmal dilatations. Some abnormal weakness of the vascular wall appears to be essential. Studies of capillary fragility in 80 patients with diabetic retinopathy showed that 85 per cent had abnormal fragility. Diabetes itself, however, is associated with increasing capillary fragility, as evidenced by the finding of abnormally weak capillaries in 48.5 per cent of diabetics with no retinal pathology. Ocular examinations of 286 juvenile diabetics at Camp NYDA showed no ophthalmoscopic evidence of retinal blood vessel disease, yet 9 patients had hemorrhages or pinpoint aneurysmal dilatations—1.5 per cent positive findings in patients having no visual complaints. The absence of exudates or changes in vessels other than the capillaries emphasizes the fact that the capillary changes are the first to occur. The retinal lesions in diabetes are closely related to the renal lesions described by Kimmelstiel and Wilson. Capillary aneurysms are often found in the kidney glomerulus and the typical globular, hyaline glomerular nodule of Kimmelstiel and Wilson may in fact be a hyalinized saccular capillary aneurysm. The retinal and renal lesions can, therefore, be regarded as joint manifestations of the same vascular disease.

The observation that diabetic retinopathy sometimes develops during pregnancy and then clears after delivery suggests that the increase in corticotropin found during pregnancy may be partly responsible for the retinal lesions. When rabbits with alloxan diabetes were given cortisone and corticotropin, the ophthalmoscopic picture produced resembled that of early diabetic retinopathy. Diabetic patients exhibiting adrenal hypofunction have been found to be free from retinal disease; those with retinal disease exhibited more adrenal activity than average diabetics without involvement of the retina. Dysfunction of both the pancreas and the adrenals, which seems to be present in certain patients with diabetes, affects the utilization of several of the B vitamins. Insulin is required for the formation of high-energy phosphate compounds and hence indirectly for the conversion of most of the B vitamins into their phosphorylated functionally active forms. Vitamin B_{12} deficiency in particular, though not solely responsible for the renal and retinal lesions of diabetes, seems to play an important part in their production.

The intensive investigations being made into these and other metabolic disturbances, such as lipemia or a change in mucoid metabolism, show that diabetic retinopathy, instead of being considered irreversible, is now being approached as a condition wihch it may soon be possible to retard, stabilize, or even prevent.

THERAPEUTICS

CORTISONE AND CORTICOTROPHIN IN OPHTHALMOLOGY

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Practitioner, 1955, *175:* 577–582

Cortocotrophin (ACTH) is effective only on systemic administration and has an action essentially similar to that of cortisone, but in certain cases is the more suitable preparation to use. Hydrocortisone is somewhat more potent than cortisone, but its action is similar; it is claimed that the new synthetic corticosteroids, 'meticorten' (prednisone or metacortandracin) and 'meticortelone' (prednisolone or metacortandralone) are still more potent and are less toxic on systemic administration.

These corticosteroids all have a similar action—a blocking of the exudative phase of inflammation and an inhibition of fibroblastic proliferation in the process of tissue repair. The effect is the same whether the cause of the inflammation be bacterial infection, anaphylaxis, allergy or trauma. These substances merely inhibit the response of the mesenchymal tissues to an irritant and the cause of the inflammation is not in any way influenced. Cortisone does to some extent delay the healing of wounds but of even more fundamental importance, the inhibition it effects of the usual protective tissue response may lead to the uncontrolled multiplication of invading organisms with dire results.

In intraocular disease the advantages and dangers are perhaps most clearly exemplified in the case of tuberculosis. In this disease, if the condition is allergic or exudative, cortisone may well be of temporary benefit, but if a caseating lesion be present or the eye invaded by tubercle bacilli, the use of these hormones may have disastrous consequences.

In external conditions if a corneal ulcer or abrasion is treated with an antibiotic combined with cortisone the results may be gratifying provided the antibiotic is effective against any infection which may be present. If, however, an organism is present against which the antibiotic is unsuitable an abrasion may be converted to a severe sloughing ulcer of uncontrolled severity.

With these reservations cortisone may be used locally and effectively in spring catarrh, marginal corneal ulcers and in luetic interstitial keratitis. In acute iridocyclitis the results of local or subconjunctival administration of cortisone is often good. In most types of chronic intraocular inflammations the dangers of its use are greater than its value and long term administration almost always alters the course of events to the detriment of the host.

In inflammation of the posterior segment these hormones are of less value than in iridocyclitis and local administration is useless. Systemic administration of corticotrophin or cortisone or one of its homologues is often effective in acute

choroiditis associated with vitreous opacities. Before embarking on the use of these hormones there should exist a practical certainty that the disease is not due to bacterial tuberculous infection.

Systemic administration may be indicated in Boeck's sarcoid, in cranial arteritis and in neuromyelitis optica. Up to the point of delaying wound healing cortisone may be used to combat the post-traumatic reaction of surgery and neovascularization in the cornea.

Comment: Now that the excitement of the great potentialities of steroids in ophthalmology has abated somewhat, a reconsideration of the proper position of these agents in ophthalmology is worth while. These authors stress the well-known fact that these agents block the exudative phase of inflammation and inhibit fibroblastic proliferation. They have properly stressed the inadequacies of this therapy, particularly in those conditions where interference with normal inflammatory action would be disastrous, and feel that the essential role of cortisone or its derivatives, particularly in most infective conditions in ophthalmology, is the control of the excessive inflammatory response with which this commentator heartily agrees. In other words, cortisone or its later derivatives may be used to block the excessive exudation during the initial phase of the infectious process until it can be brought under control by simultaneously employed antibiotics or chemotherapeutic agents. However, these agents should not be used in conditions such as tuberculosis for with the subsidence of this therapy the lesion may become widespread and diffuse rather than localized. Similarly, one must agree that the combination will be effective only if the antibiotic is able to overcome the infecting agent. On the other hand, if the antibiotic is unable to inhibit the growth of the infecting agent such as Pseudomonas, such therapy might actually increase the severity of the resulting lesion.

These authors have not mentioned the possibility of allowing a dendritic keratitis to develop or enhancing one which has already started, by the use of these steroids and their various derivatives.

Of considerable importance is the attention directed to the forms of iritis which do not do well with steroids, such as Behcet's disease and some chronic intraocular inflammations.

These authors have had good results with steroids in temporal arteritis. This has not been the experience of the commentor nor that of Banks Anderson and Willam Vallotton as recently reported. (Arch. Ophth. 1955, *54*: 6.)

IRVING H. LEOPOLD

DIAMOX THERAPY IN FLAT CHAMBER

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Brit. J. Ophth., 1955, *39:* 664–666

Forty-five patients in whom the anterior chamber had not reformed by the fifth post-operative day were treated with Diamox. In twenty-five cases cataract

TABLE 1

Results of Diamox Therapy in Non-Restoration of Anterior Chamber after Operation

Type of Operation	Cause of Non-restoration	No. of Cases Treated	Dose of Diamox	No. of Failures	Chamber Re-formed (No. of Days)					Total Cured
					1	2	3	4	5	
Cataract extraction	Leaking chamber with choroidal detachment	12	250 mg. twice daily	2	4	2	3	—	1	10
	Choroidal detachment with or without leaking chamber	13	250 mg. twice daily	3	2	4	3	1	—	10
Trephine for glaucoma	Leaking chamber without choroidal detachment	4	250 mg. twice daily	—	1	2	1	—	—	4
	Leaking chamber with choroidal detachment	6	250 mg. twice daily	—	1	2	2	1	—	6
Iridencleisis	Leaking chamber without choroidal detachment	6	250 mg. twice daily	—	2	2	1	1	—	6
	Leaking chamber with choroidal detachment	4	250 mg. twice daily	—	2	1	1	—	—	4

extraction had been done, in ten trephine, and in the remaining ten iridencleisis. All received 250 mg. of Diamox twice daily until 2 days after reformation of the anterior chamber or for one week when this did not occur. Treatment was successful in forty patients. The results are summarized in table 1.

Twenty-three of the cases were complicated by choroidal detachment. Thus a fundus examination should be done when the chamber has not reformed by the fifth day after operation. A possible mechanism of action of Diamox in eyes without a leaking anterior chamber is decreased pressure in the posterior chamber permitting the iris to fall back. With the reformation of the anterior chamber the choroidal detachment also disappears, through the readjustment of pressure in the various ocular compartments.

Comment: The authors report rather remarkable results in the use of Diamox therapy in the treatment of a shallow anterior chamber following cataract extraction and operations for glaucoma. Delayed formation of the anterior chamber following cataract surgery is in most instances, due to a leaking wound. There are many instances in which this is not demonstrable microscopically, even with the fluorescein test. In most cases, the shallow anterior chamber is associated with a choroidal detachment, though if one examines the fundus routinely in all cases of cataract extraction, one will find many instances of choroidal detachment in an eye with perfectly normal depth to the anterior chamber. In the reviewer's experience, Diamox has been of some value in a few cases, but the

results are frequently disappointing. There is no reason why Diamox might not be tried for two or three days, but if the chamber does not reform, one should re-suture the wound providing a leak can be demonstrated. If a leak cannot be demonstrated, one should evacuate the subchoroidal fluid by means of a sclerotomy, at the most dependent part of the choroidal detachment, and follow this by the injection of air into the anterior chamber. This is a relatively safe procedure and results, in practically every instance, of reformation of the anterior chamber.

Following filtering operations for a glaucoma, a shallow anterior chamber is not an unusual complication, especially following the trephine operation. The purpose of the filtering operation is to allow aqueous to escape into the subconjunctival space, and, if the drainage opening is adequate, or a little too adequate, one may have a large cystoid bleb developing and a shallow anterior chamber. In this type of case, it is quite probable that the reduction in the amount of aqueous formed by the use of Diamox results in less pressure in the subconjunctival space and fibrosis of the scar to the episcleral tissues may reduce the amount of area available for drainage and consequently by building up the intraocular pressure, permit the anterior chamber to form.

In the reviewer's opinion, the use of Diamox in uncomplicated cases of choroidal detachment, has not hastened the disappearance of the choroidal detachment. Delayed formation of anterior chamber following any type of intraocular surgery can prove to be a most embarrassing complication. The use of Diamox for a short period of time as a temporizing measure is permissible, but operative intervention should not be delayed unnecessarily.

P. Robb McDonald

ECONOMIC, SOCIAL AND LEGISLATIVE

THE DEVELOPMENTAL EVALUATION OF THE BLIND PREMATURE INFANT

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Am. J. Diseases Child., 1955, *20:* 135–140

A sample of 10 premature infants with blindness caused by retrolental fibroplasia, a sample of 10 premature infants with normal vision, and a control group of 80 full-term normal infants were formally tested by the Gesell method to determine whether the Gesell norms are applicable to seemingly normal premature infants and also to those that are blind, when certain corrections are made. These corrections relate to the number of weeks of prematurity and to the allowances that must be made for items in the tests in which vision alone is concerned, such as regarding the pellet or following the dangling ring with the eyes.

The mean corrected developmental quotients of the three groups were all well within the normal range and this suggests that when the proper correction is made for the weeks of prematurity, the developmental standards for full-term infants can be used in testing premature infants, whether blind or with normal vision. Further supporting evidence was provided by the answers to a questionnaire dealing with eight developmental items sent to parents of children with blindness due to retrolental fibroplasia. The replies of 28 of the parents, based on written records such as baby books, indicated that all but two grossly retarded infants followed the usual developmental pattern of full-term infants, especially when allowance was made for the weeks of prematurity. The only items in which there was a definite delay, apparently because of the need of vision for balance, were sitting without support, standing alone, and walking alone.

Comment: Following the recognition of retrolental fibroplasia as a definite entity, it was unfortunately and inaccurately reported that many of these children are also mentally defective. A large number of studies have since indicated that this error arose because of the use of testing methods in which vision played a prominent role. Undoubtedly, too, the incidence of neurologic disease and mental deficiency is higher in prematures than in full term infants, regardless of blindness. Parmalee's interesting study indicates that if allowance is made for weeks of prematurity and defective vision, most children with retrolental fibroplasia are developmentally comparable to full term sighted infants. Because of dependence on vision, sitting without support, standing alone, and walking alone are definitely delayed, whereas smiling, putting objects in the mouth, pulling to a stand, and walking while holding on follow the established norms.

Basic Sciences

OPTICS

THE PROBLEM OF FORM IN VISUAL PERCEPTION

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Am. J. Optom. and Arch. Am. Acad. Optom. 1955, *32:* 599–615

A. EARLY CONCEPTUALIZATION OF VISUAL PERCEPTION

The distinction between visual sensation and perception caused psychologists difficulty in the eighteenth and nineteenth centuries. Essentially a perception is only partially dependent upon sensations that come via the senses; the total visual experience depends upon how the various sensations are combined.

This dichotomy emphasizes the complexity of the visual stimuli and the individual differences in response. Different persons respond differently to the same stimuli and even the same individual does not remain consistent from time to time. The arbitrary distinction between sensation and perception was thus ultimately recognized as fruitless and the attempt to distinguish between them was abandoned.

During the same period the space of the universe for the philosopher and psychologist was empty Euclidean space, defined by the three dimensions of the Cartesian coordinates. Shape and form were thought of in terms of the abstract Greek geometry. This thinking was readily translated into seeking for physiologic equivalents of the geometric world within the retina. Emphasis, at that time, in the physical sciences upon finding the "elements" of matter was reflected in the behavior sciences in the search for the "elements" of sensation.

B. THE GESTALT THEORY

The Gestalt school of psychology arose out of the objection to the structuralists' interest in the search for the elements of sensation. They were strong proponents of the standpoint that any psychological experience must be studied as a "whole" (the literal meaning of Gestalt), and that something was lost when an experience was analyzed into parts.

A classical example of the Gestalt approach is in the analysis of a square into component parts. They argued that while an analysis of a square into four lines is possible, no amount of the lines taken separately would yield the quality of "squareness." Furthermore, they stressed the fact that retinal projection may

vary considerably without making any difference in the reported perception (constancy phenomena). Thus when one watches a moving car the retinal patterns change tremendously but perception remains unchanged.

Hence the Gestaltists shifted emphasis from trying to make events occurring at the retina agree with total perception and placed emphasis upon the functioning brain. Further analysis did away with the dilemma posed by the distinction between the three-dimensional world and a two-dimensional retina. Thus perception is innately three-dimensional even under the most impoverished conditions.

Gestaltists then postulated that homogenous areas of different types and patterns will produce forces at their boundaries. Abrupt discontinuity is not enough to account for these forces, but they develop within homogenous areas and tend toward simplification of that form. Additionally, forces develop external to these areas which also tend to alter their distribution. The resultant of these external and internal forces is the total perception. Further studies were directed toward those forces which made points and lines appear as particular shapes and forms.

C. CONTEMPORARY WORK

Detection, broadly speaking, refers to that level of performance that calls for distinction between nothing and something. That is, the person can vaguely report that "something" was there to be seen but could not even guess as to what it was.

Recognition, refers to the ability of not only being able to determine something versus nothing, but to identify correctly what that something is. The distinction between recognition and detection includes most contemporary work.

There are three main theoretical fields of study in contemporary psychology: total area as the main variable that determines detection; the border of the figures used as the main variable; and finally the perimeter-area group which combine the first two concepts.

Future studies would appear to be in several fields. Form, as such, is a separate problem. Line drawings, pictures, and the like, which are used almost exclusively in the research of form, may not yield results, which is true of three-dimensional vision. Knowledge is incomplete on the detection level and this information is essential. Area or border are insufficient to explain form perception, but an approach which considers both seems to be the direction in the future.

Comment: Since this article is itself a survey, it is hard to indicate its content in a condensation. The author, a psychologist, read this paper before a convention of optometrists and kept the presentation of his material, at that generally understandable level of kindness, rarely found, but highly desirable, whenever a group of practitioners is to be approached. Ophthalmologists, if interested in, but not familiar with the subject, will therefore enjoy this excellent publication and should read the original.

Ophthalmologists with their traditional training in morphologic physiology will still be inclined to think of the visual process in terms of so-called sensation, and it is this type of thinking which sired the concept of "form sense," of a faculty supposedly on

equal level with light sense, color sense, and even "space sense," the *Raum-Sinn* of the classic German "sensationalists." It will be well for them to see the weakness and the inherent insufficiency of such concepts.

As to the *Gestalt*-school, the reviewer has hardly ever read such excellent description and evaluation of its contribution in such concise manner. Equally good is the analysis of the contribution of the "contemporaries." The author well recognizes that their contribution is not all in the direction of progress and that under what one nowadays calls "detection" and "recognition" there is in fact the old hackneyed dichotomy hidden of "sensation" and "perception." Even if new data appear in the shining armor of electronic equipment and are plumed with formidable mathematical statistics they add little to our knowledge of form contributed by the *Gestalt*-school. Possibly, the most important contemporary addition to this knowledge came from the work of Fry on the visibility of borders and, of course, Gibson's studies, the essence of which is also competently reviewed.

ARTHUR LINKSZ

COMMONPLACE VIEWING AND DEPTH DISCRIMINATION

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J. Optical Soc. Am. 1955, *45:* 913–918

In a previous study it was found that for daytime observations commonplace depth discrimination depends strongly upon viewing distance. The present study was made under arctic conditions, near Churchill, Canada.

The subjects were four soldiers with normal vision and depth perception as measured on the Howard-Dolman test. The apparatus consisted of a variable target, a rectangle 66 x 72 inches mounted on a tracked vehicle (type Weasel) so as to conceal the vehicle from front view and a fixed target the same size mounted on the ground.

The trials were administered with the subject a selected distance from the fixed target. The movable target was started a variable distance from the standard and moved at the slowest possible speed toward the standard. The subject waved a red flag when the two targets appeared to be equally distant.

The results indicated that within a range of 100 to 3000 feet the precision of depth discrimination related to observation distance. Statistical analysis did not reveal a significant difference between binocular and monocular vision except that at 750 feet binocular vision was consistently superior. Comparison of the difference in precision between monocular and binocular viewing showed that in most out-of-doors situations the precision is improved considerably compared

to what would be expected on the basis of stereoscopic vision alone. With the aid of both binocular and monocular cues the precision of depth perception is increased 95 per cent at an observation distance of 200 feet over precision based upon stereopsis alone. The results suggest that stereoscopic vision makes only a slight contribution to the precision of depth discrimination although it may be very important in producing a feeling of depth.

The authors hypothesize that the major cue for commonplace depth discrimination is alignment in the heights of the target images, or vernier image alignment.

Comment: This is a very important paper which should be studied in the original. It is high time that stereopsis is put into its proper place and that the guilt complex of the mothers, who think their children see everything "flat," in the cases without stereopsis, be reduced. However, as can be expected from those proposing an unorthodox view, the authors have overdone their argument somewhat. Even if stereopsis is not as important as some of the more vocal proponents of "visual training" would like the public to believe, it is not as insignificant as the authors want us to assume. Accepting for a moment as valid the mathematical *tour de force* by which the authors seek to prove that at a distance of about 200 feet in common place environment depth discrimination is 95 per cent more precise than pure stereopsis, one can deduce from their formula with equal validity that stereopsis gives even at 200 feet at least 51 per cent of all the relative depth clues. And if it is correct that the precision of stereopsis *decreases* by the square of increasing viewing distance, than it seems an equally valid deduction from the same equation that the precision of stereopsis *increases* with the square of approach. It is all a matter of emphasis. Automobile drivers, airplane pilots, ophthalmic surgeons can do very well in commonplace environments even without the faculty of stereopsis. The first two might do equally well at their jobs as those who have it since stereopsis is limited in scope to distances not greater than about 2000 feet (as recently shown by Ogle, Graham and this reviewer). The surgeon not as well, since he is lacking the equipment for clues which even according to the author's formula constitute at least 51% of all close range depth clues. Stereopsis is not the refinement of one's vernier-setting ability. To give one example, no one can ever set the targets of the space-eikonometer without the faculty of stereopsis. This is an all-or-none, not a gradual affair for which the presence of a peculiar physiologic equipment is necessary. It is neither acquired nor learned, nor for that matter, a refinement of some of faculty or some form of elaboration on some higher mental level. One can, however, certainly live and function without it, as well as, say, without the equipment for red and green discrimination.

It should be noted that the authors' equation from which they deduce that depth perception is improved by monocular depth clues at 200 feet distance by at least 95 per cent, leads to a curve which asymptotically flattens at about 2000 feet. Thus, from here to infinity, the share of stereopsis should offer a constant 50 per cent of all clues. This, obviously, contradicts the views of Ogle and Graham quoted by the authors. At least in the case of ordinary human pupillary distance, the value of stereopic clues decreases to zero with increasing distance. The pupillary distance is a parameter which cannot be left out in the mathematical treatment offered by the authors and they have themselves reintroduced it in their discussion.

ARTHUR LINKSZ

THE X-RAY AND RADIUM PHOSPHENES

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Brit. J. Ophth., 1955, *39:* 577–598

It is well known that radium radiations and x-rays can produce a sensation of light on striking an individual's eye. This phenomenon is being used clinically to locate foreign bodies within the eye and to test the retinas of eyes with cataracts. It has recently been used to measure the diameters and refractive power of living human eyes.

The phosphene produced by x-irradiation of the entire eye has been described as a homogeneous luminous glow, filling the entire visual field. Light and x-ray phosphenes have a number of similarities. All investigators have found that the eye must be dark adapted before x-rays can be seen. Stimulation of the eye causes a direct pupillary reflex and a consensual reflex in the opposite eye. Early studies showed that x-rays stimulated electroretinographic action currents within the eye of experimental animals.

The color of x-ray phosphenes varies with the current used and appears brighter in the peripheral than in the central field. X-ray phosphenes are not refracted by the ocular media to form an image on the retina. The images formed by x-rays arise because of the silhouetting of objects against an x-ray source.

Studies by the author indicate that rods are excited by x-rays. However, he points out that since the x-ray phosphene is seen in colors other than the desaturated blue of rod dominated vision, cones too must be affected. The radium phosphene consists of two parts: one caused by beta particles and a much dimmer one caused by gamma rays. The beta particles act by producing fluorescence within the eye and the gamma particles (like x-rays) by stimulation of the rods and cones.

Comment: This paper concerns the subject of the author's thesis at the University of California. The voluminous literature concerning this fascinating topic is extensively reviewed. One's first reaction is that of morbid curiosity concerning the development of radiation cataract in the intrepid early investigators and their unsuspecting subjects. Probably the dosage available with the early apparatus was too small to give rise to later difficulties.

The most useful information derived from application of the unusual properties of x-ray phosphenes has been the measurement of the diameters of the living eye. By directing a narrow bean of x-rays into the eye from the temporal side, it is possible to find that point at which the posterior pole is stimulated. A measurement of the position of the anterior surface of the cornea and the position of the x-ray beam gives the axial length of the globe. Stenström (English translation, Am. J. Optom., 1948, *25:* 218, 286, 344, 388, 438, 496) used this information to correlate the axial length of the eye with the refractive error,

curvature of the cornea, depth of the anterior chamber, and curvatures of the lens in a series of individuals with refractive errors of less than one diopter. His monograph, which deserves to be read in full, most decisively indicates the correlation existing between the refractive power of the anterior segment and the length of the globe to give a nearly emmetropic eye. A large number of similar experiments suggest themselves: studies in myopia with degeneration, in hyperopia of more than eight diopters, comparison of the two eyes in aneisekonia, and the like.

BACTERIOLOGY

RATE OF STERILIZATION AS A FACTOR IN THE SELECTION OF OPHTHALMIC SOLUTIONS: EXPERIMENTAL STUDIES WITH A PROPOSED METHOD OF PREPARING STERILE SOLUTIONS

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A.M.A. Arch. Ophth. 1955, *54:* 725–732

The concept that bacteriostatic concentration levels present adequate preservation for ophthalmic solutions appears to be a generally accepted view. It is the level of preservation found in proprietary ophthalmic preparations. The authors contend, however, that bacteriostatic concentration levels present an inadequate margin of safety, when the ophthalmic solution is used by the physician in his office, emergency treatment room, clinic, surgery or hospital ward. The point of disagreement rests, critically, on a consideration of the time period of exposure required to sterilize the solution.

Laboratory experiments were conducted on the basic premise that a laboratory in vivo test method could serve as a means of evaluation of sterility. An ideal in vitro test might detect a single living bacterium but a test procedure utilizing a poor chemical antagonist might be falsely interpreted as being sterile. Experimental infections of Pseudomonas aeruginosa can be established in nearly 100 per cent of inoculated eyes and produce a fulminating type of infection.

Experimentally, a one cc. quantity of a 24 or 48 hour broth culture of P. aeruginosa was added to nine cc. of a sterile saline solution of the bacterial agent being tested. The bacteria were exposed to the test solution for periods varying from five minutes to one week. At varying periods the contaminated test solution was injected intracorneally into rabbits eyes or added to culture solution.

Phenylmercuric nitrate, in concentration of 1:10,000, showed growth of the test organism after one week exposure and was judged to be inadequate against P. aeruginosa in ophthalmic solutions. Benzalkonium chloride in concentrations less than 1:5,000 was found to be lacking in bactericidal and bacteriostatic activity after 24 hours contact. Chlorobutanol possessed activity under proper conditions of handling but positive cultures were found four to six hours after contamination. Polymixin B consistently sterilized heavily contaminated solutions in less than 30 minutes. It is not a broad spectrum bactericide and additional antibacterial agents must be incorporated. The rapid action of benzalkonium chloride against Gram-positive organisms makes it the additional agent of choice. Benzalkonium chloride is incompatible with nitrates, salicylates, fluorescein and the sulfonamides. It is suggested that Polymyxin B sulfate

(1000 units per cubic centimeter) be combined with 1:10,000 benzalkonium chloride in ophthalmic solution where chemical incompatibility is not present.

Comment: The authors' contention that a bactericial effect is essential in preservatives for ophthalmic solutions must be evaluated in the first place with due regard for other properties to be looked for in the ideal preservative, and secondly, with a view to the circumstances under which solutions containing a given preservative are to be used. Since viral as well as bacterial contamination of solutions can occur, collyria administered by medico personnel in the routine of the clinic must be handled with strict aseptic precautions. As the authors note, this involves the use of an individual sterile dropper each time a bottle of an eye solution is entered. Under these conditions, it appears that the technique of handling rather than a rapidly batericidal preservative is the essential factor. A preservative which is merely bacteriostatic may be preferred on the basis of other properties.

In the presence of a break in the corneal epithelium, only solutions of known sterility should be used. The only guarantee of sterility is that the solution shall be presented unopened after autoclaving, or shall contain a mixture of antibiotics (including polymyxin) certified as sterile by the manufacturer. Such a mixture should be used in addition to any other solution when the corneal epithelial barrier is broken.

Solutions for use in the anterior chamber must be both sterile and innocuous to the corneal endothelium. The use of benzalkonium chloride as a preservative is excluded under these circumstances. The authors offer no statement regarding the effect of polymyxin on the endothelium.

When a solution is intended for prolonged use by an individual patient, the factor of sensitization takes precedence over bactericidal effect. While it is assumed, with some reason, that sensitization by polymyxin is rare, one may question the wisdom of exposing large numbers of patients to this risk, no matter how slight it may appear.

The use of in vivo as well as in vitro technique by the authors is praiseworthy, and it is of interest that they found the living rabbit's cornea to be an excellent culture medium for the detection of small numbers of Pseudomonas organisms.

Even if the authors' premise be accepted in principle, acceptance of their conclusions must be withheld pending demonstration of (1) the influence of variations in pH on the bactericidal effect of the preservatives recommended by them, (2) proof that this bactericidal effect is not impaired by combining the preservatives with each other and with common ophthalmic alkaloids in solution, and (3) evidence that this combination of preservatives is both effective and innocuous under actual conditions of clinical use.

HENRY F. ALLEN

BIOCHEMISTRY

CATARACTS INDUCED BY ALLOXAN DIABETES IN RATS AND RABBITS: EXPERIMENTAL STUDIES

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A.M.A. Arch. Ophth., 1955, *54:* 564–572

The present study was undertaken to determine whether the progress of cataract formation, when induced by diabetes in rats and rabbits, can be altered by the following procedures: (1) feeding of diets containing an excess of nicotinic acid, (2) the injection of cysteine, or (3) maintenance of the animals in an atmosphere of 38–40 per cent oxygen. A comparison was also made of cataract formation in rats and rabbits as observed with the ophthalmoscope. Finally, the lenses were examined histologically for the purpose of supplementing and verifying the observations made in the other studies.

Adult male rats were made diabetic by the injection of alloxan and the blood sugar, urine volume, food intake, and body weight were followed. One-half (13) of the paired animals were given a synthetic stock diet and the other half were given the stock diet plus 0.1 per cent nicotinic acid. For the cysteine investigation, one-half of the diabetic animals in the group were injected subcutaneously with 35 mg. of freshly neutralized cysteine twice daily. In the third part of the study, animals were placed in a chamber containing from 38 to 40 per cent oxygen. The animals were placed in this chamber immediately after the injection of alloxan. Since the rats were not in individual chambers, the food intake of each animal could not be compared with that of a control. The rate of cataract progression in these rats was compared with that in rats which had similar signs of diabetes but which were maintained in the normal atmosphere.

Albino rabbits weighing between 1.5 and 1.8 kg. were injected intravenously with 100 to 120 mg. of alloxan per kilogram of body weight. The optimum dose was 120 mg./kg., since smaller doses did not make the animals permanently diabetic.

Both rats and rabbits were examined ophthalmoscopically at weekly intervals. The lens opacities were graded one plus to four plus, as in an earlier study, and an attempt was made to localize the lesion in the lens.

Ophthalmoscopic study of the diabetic rats showed unmistakable evidence of a direct relationship between the blood sugar levels and the development of diabetic cataract. A definite arithmetic progression reported by another investigator, however, was not reflected in these findings. The first change observed was either an anterior or a posterior subcapsular opacity, the former being the

more frequent. Occasionally, equatorial vacuoles were the first evidence of cataract. When they were seen, they were usually followed within a week by anterior or posterior subcapsular opacities. These opacities enlarged, frequently appearing to follow the suture lines, and subsequently anterior or posterior cortical changes developed; occasionally, the two appeared simultaneously. These subcapsular and cortical changes increased and extended to the periphery of the lens, and eventually no fundus reflex could be seen. If the severely diabetic animal was allowed to survive, the lens in most instances became swollen and contained water slits.

In general, it required a longer period of time for lens opacities to develop in diabetic rats when their blood sugar levels were low. Cataracts did not progress beyond the 1 plus stage in any animal with blood sugar levels below 300 mg./100 ml. Furthermore, lens opacities did not develop in 10 animals that had blood sugar levels between 100 and 300 mg./100 ml., although they were followed for 20 weeks.

There was a negligible difference in the rate of cataract formation in the animals fed a stock diet and those fed the same diet with a supplement of 0.1 per cent nicotinic acid. The development and progression of cataract were similarly unaffected by either the injection of cysteine or continuous exposure to 38–40 per cent atmospheric oxygen.

In contrast to the finding in the rat, the first lens change observed ophthalmoscopically in the alloxan-diabetic rabbit always appeared first at the equator. The initial abnormality found on histologic study in both rats and rabbit lenses was a change in the equatorial region, consisting of swelling of the fibers and the separation of the fibers by small and large vacuoles; disarrangement of the nuclei of the cells of the growing fibers, evidence of degeneration in some of the nuclei, swollen fibers beneath the epithelium and also beneath the posterior capsule. The earliest change observed in the epithelium consisted of alterations in the nuclei, some of which were pyknotic and others large and pale-staining. Later there was a complete loss of some nuclei. Hyperplasia of the epithelium also appeared in the more advanced stages of cataract formation in some lenses. In about half the lenses studied, however, particularly those having 1 plus or 2 plus cataracts, the epithelial cells showed no apparent damage. Some improvement of cataractous changes was observed in certain diabetic animals when there was a gradual lowering of the blood sugar levels. This improvement, which occurred first in the equatorial zone, was confined chiefly to the superficial fibers. It appears, therefore, from the findings in this study, that the histologic changes in the lenses are not always directly correlated with the blood sugar levels found in the diabetic animal. Furthermore, there is very little relationship between the length of the diabetes, in weeks, or the duration of one plus cataract and the histologic changes. This suggests that a factor other than the high blood sugar *per se*, probably the defective utilization of glucose, is responsible for the injury to the lens.

Comment: Cataracts in the adult diabetic were first described in 1798 and in the intervening century and a half a mountain of literature has accumulated, trying to explain

the mechanism of this disorder of the lens. A great step forward was made in 1943 when Dunn, Sheehan and McLetchie (Lancet 1, 484) reported destruction of the islets of Langerhans in the pancreas by the intravenous administration of alloxan in rabbits. This provided a ready experimental animal whose diabetes could be made mild or severe by the administration or withholding of insulin. Bailey and others in 1944 were the first to report cataracts in the rabbit following the administration of alloxan. Bellows and Shoch (Am. J. Ophth. 33, 1555, 1950) and Patterson (Am. J. Ophth. 35, 68, 1951 supplement) concluded that the cataracts were related to the level of blood sugar attained. In this paper Bounds and his co-workers, find a similar pattern although not as close a relationship as had been shown by the others. A rather surprising finding also, in this paper, is the lack of protection afforded by cysteine. Since von Sallmann (as quoted in the paper) has demonstrated the protective effect of cysteine and since there is a definite decrease in glutathione in the lens with the administration of alloxan one would have surmised that here, if anywhere, supplementary SH groups would have exercised a beneficial effect. This is apparently not so. One can only conclude that 2 + 2 = 4 only in a closed system where all twos are alike and preferably dead.

DAVID SHOCH

ADSORPTION OF THIOCYNATE TO THE PLASMA PROTEINS WITH SPECIAL REFERENCE TO THE DISTRIBUTION OF THIS ION BETWEEN AQUEOUS HUMOR AND PLASMA

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Brit. J. Ophth. 1955, *39:* 681–684

Kinsey and Palm (A.M.A. Arch. Ophth. 1955, *53:* 330) described the kinetics of penetration of two ions, sodium and thiocyanate, into the aqueous humor, and concluded that there is a fundamental difference in their modes of penetration; the thiocyanate ion penetrating by "diffusion" and the sodium penetrating by "secretion."

This difference depends upon the different steady-state distributions between plasma and the aqueous humor that are apparently reached by the two ions, sodium giving a ratio: concentration in aqueous humor/concentration in plasma of approximately one, while thiocyanate gave a ratio of 0.75. The low steady-state of thiocyanate in the past would have been attributed to the adsorption of this ion to the plasma proteins, so that only 75 per cent would be freely diffusible.

However, Kinsey and Palm stated that this adsorption of thiocyanate is only apparent resulting from the presence of some other material, which has chemical reactions similar to those of thiocyanate, that is adsorbed or chemically united to plasma proteins.

To test this statement, plasma was dialysed against steadily increasing concentrations of thiocyanate in isotonic saline with the following results:

Final concentration in saline (mM)	.405	1.12	2.83	6.35
Dialysis—ratio	.73	.74	.75	.795

A decrease of the concentration of thiocyanate in saline yielded the following results:

Final concentration in saline (mM)	0.67	0.375	0.23	0.12	0.04
Dialysis—ratio	.76	.70	.715	.675	.595

These findings make it clear that thiocyanate is indeed bound by adsorptive forces to the plasma proteins, and the proportion so bound is in the order of 25 per cent. The kinetics of penetration of sodium and thiocyanate are thus likely fundamentally similar although present techniques do not permit conclusion that they are identical.

Comment: The last contribution made by Jonas Friedenwald to the ophthalmic literature was an article which appeared in the Archives of Ophthalmology for December 1955 in which he and Bernard Becker developed a mathematical theory for the formation and flow of aqueous humor. A large portion of their thesis was based on the data presented by Kinsey and Palm on the transfer of sodium and thiocyanate ions into the eye. It is this data that Davson criticizes in the paper here condensed. Davson's publication is thus of added importance since if the basic data of Kinsey and Palm are in doubt, a portion of Friedenwald's and Becker's argument must "pari passu" be questionable. The editor awaits with interest Kinsey's reply to Davson.

DAVID SHOCH

INFLUENCE ON CORNEAL PERMEABILITY OF BATHING WITH SOLUTIONS OF DIFFERING REACTION AND TONICITY

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Brit. J. Ophth., 1955, *39:* 463–473

The commonest method of investigating the permeability of the cornea is to bring a solution of the test substance into contact with its epithelial surface and to measure how much penetrates into the aqueous humour or into the stroma of the cornea itself. Clearly, it is desirable to know what range of properties of the test solution may be tolerated without causing changes in the property that is being measured.

One such property, about which disagreement exists, is the tonicity of the

solution. It was decided to reinvestigate the problem by determining the penetration of ^{24}Na into the eye from solutions of differing tonicity.

The experiments described here show no evidence of an increase in epithelial permeability over the range of tonicity 0.9 to 10 per cent NaCl. Hypotonic solutions did, however, cause a rise in permeability described previously. It was also found that an increase in the tonicity of the bathing solution in the neighbourhood of 0.9 per cent NaCl caused an increase in the permeability of the corneal endothelium, that is, of the cellular layer covering the cornea on the side remote from the solution. Whether this increase was a result of damage to the layer or an active process was not determined.

Of the 54 standard epithelial permeabilities measured in these experiments, 50 are included in the range 3 to 9×10^{-4} cm./hr. These values are less than one-half of those which were thought to correspond to normal undamaged corneas in the previous investigation. The reason for this difference has not been discovered, since attempts to reproduce the earlier experimental technique exactly have failed to give the higher permeabilities. Consistently lower values have been obtained recently, however, although small systematic variations still seem to occur.

The measurements of the endothelial permeability show a greater regularity. The value of the ratio a_a/a_e after 10 min. in 1951 was 5.6 compared to the average of 5.2 found for 29 first eyes. The value then calculated for the endothelial permeability, 0.072 cm./hr., does not, therefore, need to be revised.

The epithelial permeability to Na is resistant to large changes in pH and is independent of the total Na concentration, over a 30:1 range. This is in contrast to the frog skin where Na is known to be actively transported inwards and where the permeability is sensitive to changes of concentration and pH and it is difficult to believe that any active mechanism would be unaffected by these variations. The greater part of the movement of Na inwards across the epithelium, then, is probably determined by a passive resistance to diffusion; as previously suggested this may lie in the extracellular spaces of the wide flat cells of its outer layer.

There is a similarity in the behavior of the limiting layers of the cornea when osmotic differences are produced across them. When the solution bathing the eye is made hypotonic to the stroma the permeability of the epithelium is increased, and when the aqueous humour is made hypotonic to the stroma by bathing the eye with a concentrated solution the permeability of the endothelium is increased. In both cases this increase does not go beyond a certain limit as the tonicity difference is made greater. This behavior and the magnitude of the raised permeabilities are very similar to those observed when the fluids bathing the layers are continuously stirred. The ten-fold increase in the permeability of the epithelium which results is almost certainly an indication of damage, and it is tempting to apply the same explanation to the endothelium. The mechanism which causes the damage might be an early stage in that which was shown to rupture whichever cellular layer was facing the hypotonic solution when the two sides of an excised cornea were bathed with solutions of differing tonicity.

There is no firm ground for supposing that the raised permeability of the

endothelium is a result of damage, however, nor for drawing any conclusions as to the tonicity of tears or of the most physiologic test solution. An alternative explanation, for example, could be that the changes in this permeability are connected with a mechanism for maintaining the normal hydration of the cornea.

The pharmaceutical application of these studies is that concentrated solutions brought into contact with the eye are unlikely to cause any damage by their osmotic force; in any case, if drops are instilled they are probably soon diluted by tear fluid. If it is desired to build up a large concentration of an ionized substance in the eye, the concentration that should be instilled is the maximum that will not cause discomfort, the equivalent of 1.5 to 2 per cent NaCl. Drops of higher concentrations may stimulate a flow of tears and wash the substance off the cornea. Similarly, if there is any benefit to be obtained in altering the reaction of the drops this can be done without harm to the cornea within the range pH 4 to 10, but discomfort and flow of tears may result from exceeding the range pH 6.6 to 9.

Comment: This article again illustrates the aphorism that nothing is so certain in biology as change. Starting in 1942, Cogan and Kinsey at the Howe Laboratories at Harvard performed a brilliant series of experiments showing that, although the cornea was permeable to water, it was impermeable to most other substances, including NaCl. Therefore, the NaCl in the cornea was presumed to come from and return to the limbal capillaries. This plus the hypertonicity of the aqueous and tears caused a flow of water from the stroma into the aqueous and tears. It was this constant dehydration of the cornea that kept it transparent and clear. (Arch. Ophth., 1942, *27:* 466; 1942, *28:* 272, 449, 661; 1944, *31:* 408).

This was a delightful theory and explained almost all the known characteristics of the cornea. Unfortunately Potts (Amer. J. Ophth., 1950, *53:* 504, and 1953, *36:* 127) showed that the endothelium *in vivo* was permeable to sodium and Maurice in two preceding papers (J. Physiol., 1951, *112:* 367 and Brit. J. Ophth., 1951, *35:* 791) and again above confirmed the work of Potts. (It should be mentioned in passing that in 1954, at the meeting in New York of the International Congress, Kinsey very beautifully reconciled the objections to his theory and further comment will be made when this article is published.) In the present paper Maurice points out that alkaline solutions (above pH 10) increase the permeability of the cornea enormously and this fact, plus their lipid solubility, is responsible for the devastation that results from the application of strong alkalis to the cornea.

DAVID SHOCH

Classics of Ophthalmology
JAMES E. LEBENSOHN, Editor

A NEW DISCOVERY TOUCHING VISION

PRIOR EDME MARIOTTE

Dijon, France

Translation by Justel, Royal Soc. of London, Philosophical Trans., 1668, *3:* 668–671

Having often observed in anatomical dissections of men as well as brutes, that the optic nerve does never answer just to the middle of the bottom of the eye, i.e., to the place where is made the picture of the objects, we directly look on; and that in man it is somewhat higher, and on the side towards the nose; to make therefore the rays of an object to fall upon the optic nerve of my eye, and to find the consequence thereof, I made this experiment:

I fastened on an obscure wall about the height of my eye, a small round paper, to serve me for a fixed point of vision; and I fastened such another on the side thereof towards my right hand, at the distance of about two feet; but somewhat lower than the first, to the end that it might strike the optic nerve of my right eye, whilst I kept my left eye shut. Then I placed myself over against the first paper, and drew back by little and little, keeping my right eye fixed and very steady upon the same; and being about 10 foot distant, the second paper totally disappeared.

That this cannot be imputed to the oblique position of the second paper is evident in that I can see other objects further extant on the side of it so that one would believe the second paper were by a flight taken away, if one did not soon find it again by the least stirring of one's eye.

This experiment I made often, varying it by different distances, and removing or approaching the papers to one another proportionally. I made it also with my left eye, by keeping my right eye shut, after I had fastened the second paper on the left side of my point of vision; so that from the site of the parts of the eye it cannot be doubted but that this deficiency of vision is upon the optic nerve.

This discovery I communicated to many of my friends who found the same thing though not always just at the same distances; which diversity I ascribed to the different situation of the optic nerve. You have made it yourself in His Majesty's library where I showed it to those of your illustrous assembly; and you, as well as I, found the like variety, there being some, who at the distances mentioned lost the sight of a paper, 8 inches large, and others who ceased not to

see it but when it was somewhat less; which appears not how it can be caused but by the differing magnitudes of the optic nerve in different eyes.

This experiment hath given me cause to doubt whether vision was indeed performed in the retina (as is the common opinion) or rather in that other membrane, which at the bottom of the eye is seen through the retina and is called the choroid. For if vision were made in the retina, it seems that then it should be made wherever the retina is; and since the same covers the whole nerve, as well as the rest of the bottom of the eye, there appears no reason to me, why there should be no vision in the place of the optic nerve where it is: on the contrary, if it be in the choroid that vision is made, it seems evident that the reason why there is none on the optic nerve is because that membrane (the choroid) parts from the edges of the said nerve and covers not the middle thereof as it does the rest of the bottom of the eye.

Upon this I desire you would give me your thoughts with freedom since I am none of those that love to obtrude conjectures for demonstrations.

DISCUSSION BY MONSIEUR PECQUET

Everyone wonders that no person before you hath been aware of this privation of sight which everyone now finds after you have given notice of it. But as to the sequel you draw from this discovery, I see it not cogent to abandon the plea of the retina being the principal organ of vision. For (not to insist here on other considerations) it will be sufficient now to take notice that at the place of the optic nerve there is something that may very well cause this loss of the object. There are the vessels of the retina, the trunks whereof are big enough to give a hindrance to vision. These vessels, which are no other but the ramifications of the veins and arteries, are derived from the heart, and having no communication with the brain, they cannot carry thither the species of the objects. If therefore the visual rays issuing from an object fall on these vessels at the place of their trunk or main body, 'tis certain that the impression made thereby will produce no vision and that the picture of that object will be deficient. It is not so in respect to the small ramifications that issue from those trunks and shoot into the retina; for if they be met with at the place of the bottom of the eye where vision is made distinct, they will not render the image of the object deficient because they are so small as not to be sensible.

Comment: The discovery of the blind spot was not a matter of chance. Mariotte had observed in animals the nasal entrance of the optic nerve and then set about determining the sensitivity of that area. When he found this insensitive to light he concluded that the vascular choroid was the percipient coat because of its absence at the disk, and in this opinion Mery concurred. The error was definitely rectified by Helmhotz, who showed that nerve fibers themselves are incapable of sensation.

Thomas Young in 1800 gave the first exact measurements of the visual field and of the blind spot. Von Graefe, the father of clinical campimetry, noted in 1856 the enlargement of the blind spot in disease. The extent of the blind spot is such that "at a distance of fifty feet a human figure would disappear completely" (Bjerrum). One-eyed drivers are not handicapped thereby because of the physiologic fixation nystagmus.

Because of the latent period of response the extent of the blind spot is less when tested centripetally than in a centrifugal direction. Both measurements should be made and the mean taken. Exploration should be perpendicular to its borders. Continuing from the nasal to the temporal border is an error which causes the blind spot to be displaced temporally. Diminution of the test object or of luminance enlarges the blind spot and reveals adjacent scotomata more readily. A black test object on a white field gives a blind spot 6 per cent larger than the reverse contrast. The blind spot in uncorrected aphakia is one-third larger than normal. In alleged monocular blindness the demonstration of the blind spot with the "blind" eye covered, but not with both eyes open, is presumptive evidence of malingering.

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BIOGRAPHICAL NOTE

Edme Mariotte (1620–1684) lived most of his life at Dijon where he became prior of St. Martin-sous-Beaune. He was an original member of the Academy of Sciences founded in Paris in 1666, and his reports concerning the discovery of the blind spot was presented in an exchange of letters between two fellow members. His subsequent letter gave the diameter of the largest disk of paper that could disappear completely from sight, and Mariotte insisted "that the whole area of the point of entrance of the optic nerve is blind." Mariotte easily explained the imperceptibility of the blind spot in binocular vision but in monocular vision he was puzzled to observe that, instead of the expected dark spot, the color of the background covered the unseen area. Helmholtz mentions that Mariotte demonstrated his experiment before Charles II of England. Unfortunately this statement which is historically untrue, was originally based on a misreading of an abbreviated Latin footnote in Haller's *Textbook of Physiology*.

The great variety of physical subjects to which Mariotte contributed included the nature of color, the notes of the trumpet, the motion of fluids, the freezing of water and the recoil of guns. He proved that it was the reflection of light that caused an eye to be luminous. He anticipated Auenbrugger in recognizing the clinical value of percussion. His "Essais de Physique" contains a statement of Boyle's Law which he discovered independently a few years after Boyle, but which is still called Mariotte's Law in France. He was the first to demonstrate that the rate of falling in a vacuum is the same for a coin and a feather. Condorcet said, "It is Mariotte, who first in France introduced into physics a spirit of observation and of doubt."

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Reports from Abroad

BELGIUM

The Ophthalmologic Clinic of the University of Ghent is interested especially in gonioscopy, on which subject two studies have recently been published (Advances in Ophthalmology and Glaucoma); special studies have also been made of heredity in ophthalmology, which has made it possible to isolate a dermochondrocorneal syndrome, a polar and posterior cortical cataract and a new form of corneal dystrophy. Other subjects receiving special attention include toxoplasmosis and uveitis, the pathologic histology of the eye, ocular tumours, etc.

Among the problems to which special investigations have been devoted, the following are outstanding:

Dr. M. Rabaey has made a special study of the proteins of the lens. Investigations with the aid of paper electrophoresis have shown that, in the various animal species, there are usually three protein fractions; man and various apes show four fractions. In man, the various fractions are well-defined only in the very young. With advancing age (15 to 20 years) the electrophoretic patterns become vaguer and well-defined fractions are no longer found. There is no longer a difference between the normal and the cataractous crystalline lens. Other investigations, by immuno-electrophoresis and by ultracentrifugation, have shown that the number of protein fractions is in fact considerably larger. There are differences in pattern and distribution of the various protein fractions between various animal species. It is there of significance that, in all mammals, the same protein is found, which corresponds with α-crystallin and has a very high molecular weight—considerably higher than any other crystallin protein. By means of a new fractionation technique this protein has been prepared in powder form.

Electrophoretic and immunochemical examination after ultracentrifugation showed that this protein is entirely pure. The solubility of this α-crystallin has been verified, as have also been differences between the cortical and the nuclear parts. The amino-acids were also studied, with the aid of paper chromatography, and comparisons were made with other crystallin proteins. Electrophoretic studies were made also of crystallin proteins in cataracts experimentally produced with the aid of galactose. The study of crystallin proteins in animals varying in age has made it possible to determine changes in α-crystallin on the one hand, and to find a protein produced only or mainly in the embryonic layers of the crystalline lens on the other.

Dr. Rabaey, in collaboration with Dr. A. Neetens, has also made a series of investigations with the aid of *in vitro* perfusion of the anterior chamber in human and other animal eyes. The routes of outflow of the perfusion liquid were studied microscopically. The rate of outflow, obtained by perfusion of human eyes, is

the same as that, obtained by clinical tonography (C = 0.25 and R = 4). Because the experimental conditions are not influenced by any circulatory or nervous changes, it is clear that the outflow of the perfusion fluid depends only upon anatomical conditions. The addition of hyaluronidase to the perfusion fluid has a much smaller and variable effect on the outflow in human eyes than in rabbits' eyes.

The rate of outflow is directly proportional to the depth of the anterior chamber and the factor of the chamber-depth should be considered as much for the clinical tonography as for the experimental perfusion value. In a case of wide-angle glaucoma, the perfusion, as well as the tonography, shows an increased resistance to outflow (C = 0.05 and R = 20) while the histologic examination shows at the trabeculum obvious lesions, which throw up the obstacle to the outflow.

The conclusion was reached that, at the level of the iridocorneal angle, there exists a mechanism of autoregulation which ensures that the depth of the anterior chamber is kept constant. Changes in the depth are prevented, as much as possible, by a change in the resistance of the routes of outflow. This mechanism is independent of differences in tension. The pressure of the perfusion liquid has in any case very little effect on the rate of outflow. It is only at a very marked increase in pressure that changes are found, which vary greatly from case to case. A normal trabeculum would seem to offer little resistance to outflow of aqueous humour when the anterior chamber is deep; the resistance increases to the extent to which the depth of the chamber decreases.

Dr. A. Neetens has studied the vascularization of the eye and of the optic pathways by various techniques, of which the most interesting are the Lieb-Ashton technique, (injection of neoprene latex 572, fixation in a 10 per cent formaldehyde solution or digestion by pepsin in an acid medium and subsequently by trypsin in an alkaline medium), the Spalteholz technique, which renders transparent the parts injected with Indian ink, Pickworth-Fazio's technique of benzidine staining, and the technique of microradiography following injection of thorotrast, which makes it possible to obtain magnification of 990 ×.

These techniques have enabled us to demonstrate the following new facts:

(1) Surrounding the optic disc, there are anastomoses between the capillaries originating from the optic nerve and the retinal capillaries proper.

(2) The short posterior ciliary arteries only supply the choroid; there are no anastomoses between the great arterial circle of the iris and the arterial network of the choroid; there are no arterioles at the level of the pars plana.

(3) There is a central artery of the optic nerve with an anterior and a posterior branch; the central artery of the retina supplies only this membrane.

(4) The capillary network of the optic nerve, which decreases in density from the anterior to the posterior aspect, is composed of two essential formations, viz: a longitudinal formation localized in the interfascicular space, and a transverse formation, as a rule pentagonal, which surrounds the optic bundles; the former ensures the continuity of the network, while the latter mainly governs the supply.

(5) At the level of the optic band, the nutrition of which depends on the anterior choroid artery, perforating arteries are seen coursing away from the

branches of the band and extending to other sites of the same organ. Here, the capillary network is considerably more irregular than at the level of the optic nerve.

(6) At the level of the external geniculate body, the nutrition of which depends on the posterior cerebral artery, there is a superficial anastomotic arteriolar network from which arterioles extend to the same organ. The capillary network reproduced, in spatial construction, the architecture of the retinal capillaries.

(7) Microradiographs obtained after injection of angiopac (the particles of which vary in size) into the anterior chamber showed in the scleral trabeculum clefts, which empty by orifices into Schlemm's canal; the diameter of these orifices measures more than 1.5 μ and less than 2.25 μ. If hyaluronidase is added to the contrast medium, the orifices are not distended but passage is facilitated through the clefts.

Dr. Verriest has been engaged especially in performing subjective function tests, including perimetry, photopic and scotopic campimetry, mesopic visual acuity, adaptometry, colour vision, etc. A study of the dimensions of the physiologic central scotoma in darkness, in relation to the global thresholds of perception, was followed by a comparison of the photopic and the scotopic field of vision, in pathologic conditions.

Numerous affections of the ocular fundus give a localized hemeralopia; even if the photopic field of vision is still normal, there are already deficiencies in darkness; the scotopic defects are always more marked than the photopic defects. This holds true for detachment of the retina and its sequelae, choked disc, vascular retinopathies, thrombosis and prethrombotic conditions of the central vein, central serous chorioretinitis, senile macular degeneration, retinopathy with angioid streaks, and tapetoretinal degenerations.

Neuro-ophthalmology is another field of application of campimetry in total darkness. The borders of the physiologic central scotoma in darkness in fact constitute increased gradients on which minute macular defects are amplified; therefore, the scotoma is increased in cases of latent retrobulbar neuritis, whereas in cases of compression of the optic pathways the scotoma is enlarged in one half or in one quadrant, even if the photopic field of vision is still normal.

Studies have actually been concerned chiefly with congenital anomalies of vision (essential hemeralopia, Oguchi's disease, achromatopsia and dyschromatopsia). Visual function tests in these cases have led to new observations which, for the most part, have not yet been published.

Dr. De Rouck has specialized in electrical function testing with reference to the action potential of the retina, resting potential of the retina; cerebral potentials and cortical responses to light stimuli, etc.

Under the experimental conditions used, orange stroboscopic light flashes with a frequency of 2 to 4/sec., normally causes duplication of the b wave (x wave and the scotopic component). This x-wave is not found in protanopia and total achromatopsia. The critical frequency of fusion, on the other hand, normally varies between 24 and 32 c/s.

The electroretinogram (ERG) has been studied in various affections particularly in the following:

In vascular affections of the ocular fundus, such as embolism of the central artery, variable responses are obtained, viz: absent, electronegative, subnormal and even normal. The amplitude of a b-wave in glaucoma, previously diminished, tends to increase and even to become supranormal in some cases after an intravenous injection of maxiton.

The ERG makes it possible to differentiate between degeneration of the pigmentary retinopathy type (ERG absent) and other types, but it also facilitates the making of prognostic decisions in the case of apparently isolated macular degeneration. If ERG response is absent, then a process involving the entire retinal periphery must be present—a fact which per sé predicts an unfavourable development.

The ERG is normal in a case of fundus albipunctatus cum hemeralopia. In Oguchi's disease, an entirely electronegative response is found (a wave or P III of Granit), on which is superimposed a small positive wave of the photopic type (x-wave).

By means of electro-encephalography the specific occipital response to a light stimulus, the latent period of which depends on the conductivity of the optic pathways and the basic cerebral activity, has been studied systematically in all ocular or neuro-ophthalmologic affections.

In a considerable number of cases of tapetoretinal degeneration there is no specific occipital response and a generalized affection of the encephalon characterized by diffuse and polymorphic dysrhythmia of low microvoltage, shows that there exists a common cerebroretinal substratum, based on a hereditary disorder in prosencephalic development.

In affections of the optic nerve (neuritis or atrophy) the specific cortical response is retarded or absent. In cases of choked disc it makes it possible to determine whether or not the nerve fibres are affected.

Registration of changes in the electric field occasioned by ocular movement affords a means of indirect determination of the resting potential of the retina. This is diminished in the case of microphthalmy, atrophy of the eyeball, retinal detachment, numerous cases of tapetoretinal degeneration, advanced siderosis and some forms of cicatricial chorioretinitis.

The modifications of the resting potential during light- and dark-adaptation are also studied. Normal subjects show a considerable fall. On the other hand, the fall is usually absent or considerably reduced in the case of retinal affections with an absent or subnormal ERG.

Oculography also may be used in testing the function of the extraocular muscles. In the case of complete or incomplete paralysis there may be absence of deflection of the iso-electric line, an irregular deflection of diminished amplitude, nystagmiform movements, etc. In mild or controlled paresis, changes in the tracing may be restricted to the minute movements produced by reading or by optokinetic nystagmus.

Jules François, M.D.
Professor of Ophthalmology and
Head of Clinic

Book Reviews

GLAUCOMA. A symposium organized by the Council for International Organizations of Medical Sciences. Editor, *Sir Stewart Duke-Elder*, England. Charles C Thomas, Springfield, Illinois. Cloth. pp. 349. $7.50, 1955.

The recent advances in our knowledge of the dynamics of aqueous flow have made the subject material of this symposium very timely. It is natural, therefore, that the emphasis on the nonclinical aspects of glaucoma should be greater than would be expected in a textbook. The participants in this symposium are the outstanding workers in the research on the aqueous flow and glaucoma. It is natural, also, though we wish it would be otherwise, that controversies exist in some of the basic concepts, particularly in the clinical aspects.

Duke-Elder, in this symposium, for the first time, clearly recognizes two distinct clinical entities under the heading of primary glaucoma, though at times during discussions, he gives the impression of reverting to his previous viewpoint. He maintains a distinction between mechanical and neurovascular viewpoints which other participants in the symposium tend to minimize. Friedenwald pointed out that pressure is not a physical phenomenon and must have a mechanical cause but the physiologic basis of that physical cause is not purely mechanical. The terminology of the two diseases, on a vote, was decided in favor of closed-angle glaucoma and simple glaucoma for the two entities. Here this reviewer would disagree with the choice of closed-angle glaucoma as a descriptive term which would describe only one possible phase of the disease. In lieu of a better, term, angle-closure glaucoma would be better since it indicates a process only and does not indicate whether the angle is open or not at a particular moment.

Norman Ashton's discussion of the anatomy and pathology of the drainage channels and posterior segment is outstanding. The work in which he made Neoprene casts of Schlemm's canal is reviewed. In addition, the vessels of the anterior drainage system are described. In view of our present controversy as to the site of resistance to aqueous outflow in glaucoma, whether it is in the collector channels or the trabeculum itself, it is interesting to note Ashton's comment that in normal eyes he found no tendency for the collector channels to narrow or diminish with age, nor did he find any suggestion from studies of casts, that narrowing or obliteration of the canal outlets themselves, are factors in the pathogenesis of glaucoma. The only site of vessel caliber narrowing which he found was at the point of communication between the deep scleral plexus and the episcleral plexus. There is a relatively small number of communicating vessels between the two. Ashton suggests that with aging, sclerotic changes in these communicating vessles might cause a marked resistance to aqueous outflow.

The question of the site of resistance to aqueous outflow is not by any means resolved. The studies of Bárány in regard to the trabeculum as such a site are exciting in this regard. Some of his experimental work is discussed in the symposium. Goldmann, too, believes the trabeculum to be the site of outflow resistance.

The nature and origin of the aqueous humor are handled by such outstanding investigators as Langham, Kinsey and Bárány. Goldmann discusses the fluorometric method of measuring aqueous flow and Grant considers tonography in his thorough manner. Duke-Elder disagrees with the tonographic values for the facility of outflow since he believes that the external pressure applied to the globe during tonography alters the venous pressure changes in which he believes to be the essential determinants of the facility of outflow. He feels that there is a discrepancy between the conclusions of tonography and his clinical observations in regard to the episcleral venous pressure. Goldmann, Weekers and Friedenwald, however, did not find changes in the episcleral venous pressure but made their measurements in the aqueous veins or in vessels into which the latter emptied while Duke-Elder referred to the pressure in the veins as they emerged from the sclera.

In this field of resistance to aqueous outflow, the symposium pointed up the changing trends in investigation of the basic facts regarding the aqueous outflow but that we are still not quite in the position to adequately apply these findings to glaucoma.

The material on gonioscopy is presented by Jules François. It is an encyclopedic summary of all of the statistics on the chamber angle. Unlike many of the American gonioscopists he includes capsular glaucoma with simple glaucoma as do a number of other Europeans. Aside from this minor point the field of gonioscopy enjoys a remarkable unanimity of opinion among authors the world over. Certainly no one considers the technique of value in the diagnosis of simple glaucoma. In angle-closure glaucoma it is of considerable value. It has led to a much better understanding of the difference between these two glaucomas.

Leydhecker and Kronfeld deal with the various provocative tests and Duke-Elder with the bulbar pressure test. For eyes with a narrow chamber angle, Leydhecker advises the homatropine test first, then the water test and finally the Priscol test. In simple glaucoma Leydhecker advises the following four tests in order: water-drinking, Priscol, caffein and Vasculat. The choice of tests is certainly not what investigators who separate the two types of primary glaucoma according to the chamber angle depth, would use. Kronfeld certainly would not. At any rate, the symposium indicated that the provocative tests are not as important as considered to be previously and certainly do not replace routine tonometry and clinical investigation.

Weekers and Hodgson discuss various clinical aspects of primary glaucoma. Their discussion, covering 35 pages, is necessarily brief and covers chiefly the action of various drugs.

The symposium type of discussion of this book serves to give an idea of the controversies which are usually not apparent in books by a single author whose own viewpoint is naturally expressed.

The participants of the symposium are to be congratulated. Duke-Elder deserves gratitude for a tremendous editorial job.

H. Saul Sugar

Anesthesia in Ophthalmology. By *Walter S. Atkinson, M.D.*, Associate Clinical Professor of Ophthalmology, New York University Post-Graduate Medical School, House of the Good Samaritan, Watertown, New York. Publication Number 251. American Lecture Series. A Monograph in American Lectures in Ophthalmology. Edited by *Donald J. Lyle, M.D., F.A.C.S.* Professor of Ophthalmology, College of Medicine, University of Cincinnati, Cincinnati, Ohio. Charles C Thomas, Springfield, Illinois. Cloth, pp. 101, $2.75, 1955.

The author has been recognized as an outstanding authority in ophthalmic anesthesia for many years and this brief manual is an abbreviated summation of his ideas on the subject. The chapters on the anatomy and the sites of injection of a local anesthetic are lucidly presented. The advice concerning the desirability of a tranquil atmosphere in the office, hospital and operating room is most sound, as is that regarding the administration of a test dose of pre-anesthetic medication the day prior to the operation, in order to reveal any idiosyncrasy. The smallest dose of analgesic and sedative that will produce the desired effect is advocated but the suggested average dose of barbiturate or chloral hydrate, Demerol and chlorpromazine will appear excessive to many surgeons.

No new material is presented, and regrettably a complete review of the literature is not presented. It is hoped that, some day soon, the author will expand this important subject to a full size book. For the most part the illustrations are good except that some borrowed from Cullen and a few of the author's own are cartoons and not particularly well adapted to the importance of the subject.

The Visually Handicapped Child (Les Enfants Amblyopes) *S. Delthil.* Monograph supplement, Bull. Soc. d'ophtal. de Paris. Paper, pp. 144. 1955.

Delthiel has discussed the problems involved in the education of the semi-sighted child since 1947. This present monograph features a detailed analysis of sight-saving classes on both sides of the Atlantic. In his extensive personal observations he has been most impressed by the program carried out in the various cities of the United States. The handicapped child is not stigmatized by his infirmity as the directive idea is to mingle children with defective vision with normal-sighted classmates as much as possible. More than 60,000 American children are in sight-saving classes. Their instruction under the guidance of a special teacher with specialized methods is supplemented by work in regular classrooms or vice versa with constant close collaboration between these phases. New York City, whose total school attendance is 914,453, has 909 students in 86 sight-saving classes; Chicago, with a school population of 486,367, has 400

pupils in 44 sight-saving classes. In Oakland, California sight-saving instruction extends from kindergarten through senior high school.

The first special classes for visually handicapped children were established in London in 1908 and in Strasbourg in 1911 under the leadership of Bishop Harman and of Redslob respectively. In the United States the first sight-saving classes were opened in 1913 in Boston and in Cleveland. Classes are usually limited to those whose corrected acuity in the better eye is between 20/200 and 20/50. A sharp delimitation on the basis of visual acuity is inadvisable as the child's intelligence, cooperation, will to learn and family background are equally important factors. In general the teaching of the semi-sighted should be oriented to manual or commercial vocations.

JAMES E. LEBENSOHN

THE LACRIMAL SYSTEM: CLINICAL APPLICATION. *Everett R. Viers, M.D.* Chief, Section of Ophthalmology, Scott and White Clinic, Scott and White Memorial Hospital, and Scott, Sherwood and Brindley Foundation, Temple, Texas; Professor of Ophthalmology, the University of Texas Postgraduate School of Medicine, Temple Division; Chief Oculist, Gulf, Colorado and Santa Fe Hospital, Temple, Texas. Grune and Stratton, 381 Fourth Avenue, New York 16, New York. Cloth, Pp. 159 with 73 illustrations, $7.50, 1955.

This book represents the only available monograph on the lacrimal system and, as such, it is a worth while endeavor. The material is well organized and adequately presented. The subject matter of each chapter is usefully outlined as a chapter heading. Illustrations are used freely and are a most helpful addition to the text, but it would be well to state their source in the individual figure legends.

The chapters making up the book are as follows: Physiology and pathologic physiology of the lacrimal system, the developmental anatomy of the naso-lacrimal passageways, disorders of the canaliculus, and congenital atresia of the naso-lacrimal duct. The next two chapters are concerned with the etiology of dacryocystitis and the methods of diagnosis. The management of dacryocystitis is discussed in chapters concerning the conservative treatment, external operations, and intra-nasal dacryocystorhinostomy. There is next a short discussion of lacrimal sac tumors. The book concludes with two short chapters on the lacrimal gland—one on disorders of the lacrimal gland and one on lacrimal gland tumors.

In the discussion of the various subjects, the emphasis is definitely clinical and probably rightly so. However, the value of the book would be increased by including a more fundamental histology, pathology and etiology. The best discussions are those of the surgical procedures, which probably reflect the main interest of the author. A rather obvious omission is any critical discussion of the expected results of these procedures.

Although diseases of the lacrimal gland are rare, a monograph concerning the lacrimal system should contain more than ten per cent on the lacrimal gland. This section in addition to its brevity does not contain any critical discussion, and is a bare review of the subject.

The author states that the majority of the material presented is not original and has been collected from many sources. Its inclusion in one monograph is the chief value of this book.

THEODORE E. SANDERS

OPHTHALMOLOGY, A TEXTBOOK FOR DIPLOMA STUDENTS. *Patrick D. Trevor-Roper, M.A., M.B., B.Chir. (Cantab.), F.R.C.S., D.O.M.S.* (Eng.) Curator, Department of Pathology, the Institute of Ophthalmology, London; Assistant Ophthalmic Surgeon, Westminster Hospital, Ophthalmic Surgeon, Central Middlesex Hospital and Willesden General Hospital; Chief Clinical Assistant, Moorfields, Westminster and Central Eye Hospital. The Year Book Publishers, Chicago. Cloth, pp. 656, 8 color plates, $15.00, 1955.

In recent years there has been a profusion of ophthalmic books exhaustively discussing a single disease or operation or an isolated ocular tissue. Other books have consisted of a series of chapters, each contributed by a different writer, and integrated more or less, frequently less, successfully, by an editor.

This entirely new book is a welcome change in this pattern. The entire field of ophthalmology is briefly surveyed and the lone author brings proper emphasis, lucidity and wit to the task. The material is directed toward the English diploma student but everyone—student, practitioner and teacher—will find much of value concisely presented.

The first third of the text is devoted to the basic sciences—anatomy, embryology, optics, physiology and refraction. The material is simply, briefly but completely presented with unusual clarity.

The clinical section is equally well written although here the small differences (largely semantic) between English and American thought and practice are more evident than in the basic sciences. There is little, however, that causes serious objection; blessedly another classification of retinal vascular disease is not presented.

The book is handsomely printed, is well illustrated with informative diagrams, drawings and photographs, and is printed on excellent glossy paper. All in all, it is the best advanced ophthalmology book, in English, for many a year.

OUR WONDERFUL EYES. *John Perry.* Whittlesey House, McGraw-Hill Book Co., Inc., New York. Cloth, pp. 158. $2.75. 1955.

This book is obviously directed at the younger student. It is an exposition of many basic facts, simply expressed and well-illustrated. It expresses the viewpoint of the ophthalmologist and is of interest because it may give an idea of how fundamental principles can be appropriately expressed to students at the early high school or late grade school level.

HANDBOOK OF PEDIATRICS. *H. K. Silver, M.D.*, Associate Professor of Pediatrics, Yale University School of Medicine; C. H. Kempe, M.D., Assistant Professor of Pediatrics, University of California School of Medicine; and *H. B. Brayn, M.D.*, Assistant Professor of Pediatrics and Medicine and Assistant Clinical

Professor of Pediatrics, Stanford University Medical School. Lange Medical Publications, Los Altos, California. Paper, pp. 548. $3.00, 1955.

This handbook is directed toward the medical student and the general physician. However, a surprising amount of information of direct practical value to the ophthalmologist is compressed in its many charts and tables. Normal blood chemistry values, drug indications and dosages, the indications for and the significance of various laboratory tests, the indications and dosages of antibiotics and chemotherapeutic agents, skin tests and the like are presented most concisely. A chapter devoted to disorders of the eye is competently written and is entirely adequate for the audience for whom the book is intended. The usual diseases of childhood, growth anomalies, psychological development and other specialty sections appear equally well done.

KERATOPLASTY. *R. Townley Paton*, Surgeon; Director, Manhattan Eye, Ear and Throat Hospital; Clinical Professor Ophthalmology, New York University Medical School; Vice President, The Eye Bank for Sight Restoration, Inc.; Director of Research, Manhattan Eye, Ear and Throat Hospital. The Blakiston Division, McGraw-Hill Book Company, Inc., New York. Cloth, $27.50, 1955.

There are few stories in the history of surgery as intriguing as the development of keratoplasty. Erasmus Darwin, in 1796, suggested that the operation might be performed. Reisinger first conducted experiments on animals in 1818 and was promptly accused by Elschnig of plagiarism. The author accounts the trials and tribulations that beset those first interested in this operation; the use of heterografts, homografts and autografts, the trials with penetrating grafts, the lamellar grafts, and keratectomy. Among the pioneers were great names as Elschnig, Von Hippel, Magitot, Müller, Morax, to mention only a few. In fact, the basic principles determined at that time are still valid. These early surgeons paid attention to the condition of the host and donor cornea, selection of cases, the round and square grafts, the use of sutures and splints, etc. Fortunately, a complete review of this subject has been possible without the usual encyclopedic format.

One may wonder why the anatomy and physiology of a small piece of tissue, 11 mm in diameter and 0.5 to 1.0 mm thick, should have baffled investigators for so long a time. The histologic structure of the cornea has been known for many years but the new methods of electron microscopy are now beginning to show some of the fine details of the structure of the cornea. The many physiologic secrets of the cornea are now being gradually uncovered with the aid of electronic and other devices that measure the chemical constituents of microscopic amounts of materials. To understand the pathologic processes that are present in tissues, one must have some knowledge of the normal physiologic processes that keep the tissues in a normal physiologic condition. As in any textbook, the subject of anatomy and physiology as well as pathology must be adequately covered and the author has fulfilled this accomplishment.

One of the most important factors in the development of any new surgical pro-

cedure is the selection of the proper cases in which the operation should be performed. This is usually arrived at by trial and error and then as new techniques, further knowledge of the physiology of the tissue, development of other adjuncts in therapy, the scope of the operation is gradually widened. Such has been the case in keratoplasty. No book can recount the hours spent by the surgeon in reviewing the cases upon whom he has operated. In this type of surgery there is sometimes only a fine line between success and failure. The graft may be in perfect apposition and everything appear to be progressing satisfactorily, when after a period of several months, it begins to cloud. It is only by trial and error that one at first determined in what type of cases the penetrating grafts were successful, and in what types of cases the lamellar grafts gave a satisfactory result. Then there are instances in which a lamellar graft was satisfactory and prepared the eye for subsequent penetrating graft. The secrets of keratoplasty are not all uncovered in this book, though, from the author's vast experience, one can avoid many of the pitfalls that occur to the surgeon with less experience. There is no question that the operative technique is now better than it was two or three decades ago. This has been due, in part, to better instrumentation, especially of the development of fine, sharp, steel needles, the availability of better anesthesia and akinesia, and if necessary, the use of satisfactory general anesthesia. The complications of postoperative infections have, to a large extent, been eliminated by the use of the antibiotics and the postoperative inflammatory reaction can, in many instances be adequately controlled, by the use of the corticosteroids.

In this volume by R. Townley Paton, he has recorded a large part of the author's life work. Apart from the technical procedures of the operation, the establishment of the eye bank, and the many ramifications that occur from such a foundation, are difficult to grasp. The legal technicalities concerning the donating of a cornea, the administrative details in establishing the bank, the examination of the donor material, are a few of the difficulties that are involved. Here we have a monumental work devoted to a piece of tissue no larger than a dime. The ophthalmic profession owes a debt of gratitude to Dr. Paton for assembling this material and on drawing on his large personal experience. The editors are also to be congratulated on the beautiful reproductions of his numerous illustrations.

P. Robb McDonald

Current Review

OPTICAL AIDS IN SEVERE VISUAL DISABILITY

EDWIN FORBES TAIT, M.D.

One of the major problems faced by the ophthalmologist, in his daily practice, is that of increasing the useful vision of a patient who, for one reason or another, does not have normal vision with ordinary corrective lenses. Practically all of such cases owe their lowered vision either to congenital abnormalities or to the sequelae of primary or secondary ocular disease. It goes without saying that, as a rule, it is inadvisable to spend much time in trying to aid the vision of any patient who is being treated for an acute disease process, but there are many whose reduction in visual acuity is the result of a chronic disease, such as glaucoma simplex, which is kept under control by suitable medication. These latter cases are properly included among those who are candidates for special types of visual aids.

Before discussing the precise methods of diagnosis and types of available visual aids, it may be well to classify patients presenting visual difficulties on the basis of how the various types of abnormalities will respond to given aids.

First to be considered are those individuals who owe their poor vision to irregularities of the anterior corneal surface with no great changes in the corneal stroma. Such conditions include keratoconus and irregular astigmatism from corneal injury or surgery. Contact lenses are the obvious corrective agents for these conditions and, if no other abnormalities exist, excellent vision can usually be obtained by their use.

Densities or opacities in the corneal stroma, crystalline lens, or vitreous, require other types of visual aids. It is, of course, possible to have these latter conditions co-exist with an anterior corneal irregularity, in which case, the problem becomes much more complicated. If, however, the anterior corneal surface presents no abnormalities, an increase in useful vision in the individual presenting opacities or densities in the media requires either a better definition of the retinal image or an increase in its size. A very few individuals in the low vision group will have many small media densities situated along the visual line, each of which will represent in itself a small refractive system and each of which will differ refractively from its neighbor because of size, extent, or position in the media. The net effect of the functioning of all of these small optical systems is a generalized retinal blur, which consists of many irregular overlapping diffusion circles, thus preventing the formation of a clear-cut retinal image. Occasionally it is possible to eliminate the effect of all of these refractive systems except one by the use of multiple pin-hole spectacles, designed so to permit vision through only one pin-hole at a time. In any particular case a decision as to whether or not such an appliance would be helpful can be determined only by

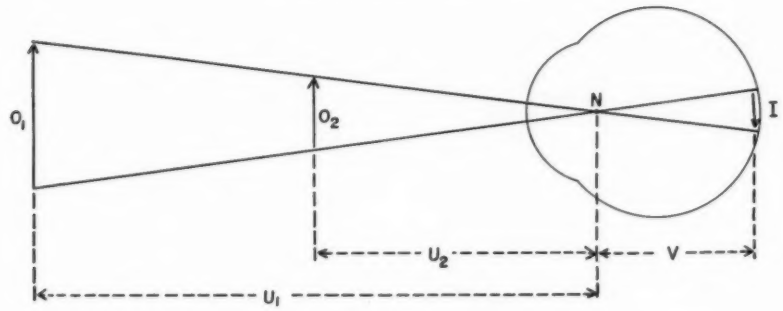


FIG. 1. Normal visual angle, showing that two objects O_1 and O_2, at different object distances, U_1 and U_2, will give the same size retinal image. The image distance V is a constant for a given eye.

experimenting with various sizes of pinholes. A set of pinhole discs, with the holes ranging in size from ½ mm. to 3 mm. by ½ mm. steps, should be part of the armamentarium of every ophthalmologist.

Pinhole spectacles, however, are not the only corrective device which can be used for this group which owes its visual deficiencies to changes in the ocular media. Frequently an increase in the size of the retinal image, with the aid of telescopic or other magnifying lens systems, will be more efficient, depending of course upon the character and disposition of the media abnormalities. Such individuals can be placed in the third classification, which includes those whose vision may be bettered by an increase in retinal image size produced by the aid of simple or compound magnifying lens systems. The design and use of these magnifying systems is the primary subject of this essay, especially that of simpler systems which may be in any optical prescription laboratory.

The effectivity of a magnifying system in producing retinal images which make it possible for the low-vision patient to increase his visual ability depends upon an increase in the size of the visual angle which is subtended by the object of regard. In a normal eye, the size of the retinal image of any object may be determined by rays from the extremities of the object converging to and crossing each other at the second nodal point of the eye and continuing on to the retina, as shown in Figure 1. The actual size of the retinal image of any object at any given distance may be determined by the simple formula

$$\frac{I}{O} = \frac{V}{U}$$

where I = size of retinal image
O = size of object
U = distance of object from nodal point
V = Distance of nodal point from retina (usually considered as 17 mm. disregarding the slight inaccuracy introduced by the intra-nodal point distance).

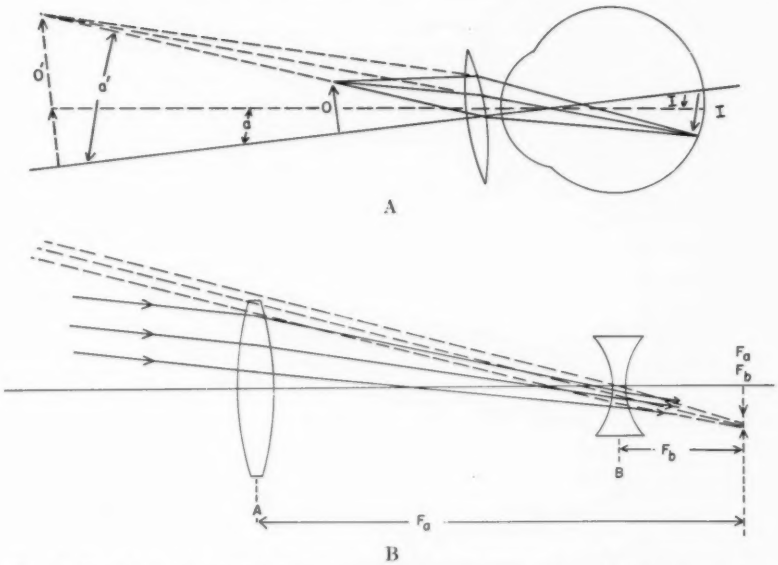


FIG. 2. Simple and telescopic magnifying systems, showing how the increase in the apparent visual angle is accomplished by a simple magnifying system. The object O located at approximately the focal point of the lens is seen by the eye as if enlarged and at O'. The lower diagram is that of a Galilean telescopic system, in which the parallel incident rays are shown by the solid lines as far as the concave ocular lens, and thence by the dotted lines, with the latter projected backward to demonstrate the increased visual angle obtained.

Magnifiers, both simple and telescopic, have as their sole function an increase in this visual angle so that the remote object seems to be brought nearer and in its new apparent position will seem to subtend a larger angle. This principle is illustrated for both simple and telescopic magnifiers in Figure 2.

Perception of size, however, is not always correlated with actual image size, and this is particularly true with objects viewed at a near point, especially if the apparent magnification, as far as the vision is concerned, is compared with the actual magnification when measured on an optical bench. It has been customary to calculate apparent ocular magnification, for near objects, as if referred to an object distance of 25 cm., thus establishing the following formula to be used for simple magnifying systems, consisting of either a single convex lens or a combination of two or more adjacent lenses:

$$M = \frac{25}{F}$$

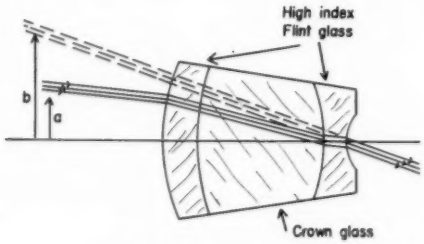
where M = Magnification

F = Focal length of lens system in centimeters.

Therefore, if a +40. D. lens which has a focal length of 2.5 cm. is used, the magnification of the system can be expressed as 10×.

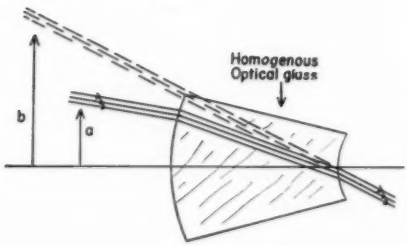
In the telescopic magnifying systems, as shown in Figure 2, there can be no specific reference distance, although magnification in such systems always produces an apparent approach of the object due to the increase in the visual angle. These systems, when designed for ocular use, are always Galilean in character, giving upright images instead of the inverted ones characteristic of the ordinary astronomical telescope, and consist of a convex object lens or single refracting surface and a concave ocular lens or surface, the two refracting surfaces or lenses being related to each other by the coincidence of their focal points. Systems such as these are the basis of all telescopic appliances for visually deficient cases, whether they be two element telescopes, Donders-Steinheil cones, or aniseikonic lenses.

Magnification in these Galilean telescopic systems is determined by the ratio of the two focal lengths. For example, a system which employed a convex object glass of 60 mm. focal length and a concave ocular lens with a focal length of 30 mm. would have a magnification of 2×. Instead of using two separate lenses, a single cone of glass or other refractive material can be made with convex and



Univis Telescope

A



B

FIG. 3. Steinheil cones. The upper cone demonstrates how the increase in the visual angle is obtained. The incident light shown by the solid lines and coming from a single point on the object at infinity, emerges from the system at an angle greater than that with which it entered. This emergent light, projected backward, determines the apparent size and position of the object in space. The lower diagram shows the optical system of a composite Steinheil cone such as that made by the Univis Lens Company. This is essentially the same as the simple cone shown in the upper diagram, except for the refractive effect at the interfaces between the elements.

concave single refractive surfaces, the convex surface having a focal length of 60 mm. and the concave surface having a focal length of 30 mm. Such a system, illustrated in Figure 3, would also have a magnification of 2×.

The principal difficulty encountered in the construction of a homogeneous telescopic system, such as the Donders-Steinheil cone, is that the convex and concave curves on the two faces would have to be of very short radius introducing some exaggerated peripheral aberrations. In recent years the Univis Lens Company has adapted a later development by Steinheil in which the classical cone is modified by using a system of three elements, cemented together, in which the outer elements are composed of high index flint glass and the middle section of a lower index barium glass, thus making it possible to use for refractive purposes the inter-faces between the elements. Figure 3 shows the cross-section of such a composite telescope.

Aniseikonic lenses, utilized for the equalization of the size of the projected retinal images in the case of individuals with aniseikonia, are actually Steinheil cones, with a much lesser separation between the refracting surfaces. Such lenses, however, are not useful in low vision cases because their magnification is limited practically to about five per cent.

INDICATIONS FOR THE USE OF MAGNIFYING SYSTEMS

In general, it is well to consider if a magnifying lens system, of one sort or another, might be useful in the case of any individual whose vision is so reduced that with ordinary corrective lenses he finds it difficult to pursue his vocation or avocation. There is no definite level of visual acuity where the need for magnification begins and no definite point at which it stops being a benefit as long as some vision is possible. Many individuals with lessened visual ability may get along perfectly well under all ordinary circumstances, but find that some help is necessary under certain special conditions.

An example of such would be an individual, seen recently, whose permanent corneal changes, brought about by interstitial keratitis, reduced useful vision to 20/50 in the better eye with a suitable lens correction. While this reduction was not sufficient to interfere with his ambulation, or even with reading, it did make it difficult for him to see the steam gauge located some 20 feet away on top of the steam boiler which he fires. In this case, a simple open telescopic system made it possible for the individual to work efficiently. At the other extreme is a patient whose vision is so defective that it is difficult for him to walk unassisted in strange surroundings, but who, with a 12× simple magnifier, can manage to read ordinary type, one or two letters at a time.

Before assuming that magnifiers are or are not needed in a given case, the patient's visual needs, his intelligence, and probable adaptability should be evaluated and considered along with his actual visual acuity as determined by trial. It should also be kept in mind that the immediate results of testing vision with magnifying systems must not be considered as those which will be obtained after the individual has had an opportunity to adapt himself to the new visual situation with the magnifying aids.

All low-vision patients should be told that learning to use magnifying appliances means that he must "learn to see all over again". Imperfections in vision are magnified, as are the objects themselves, and consequently a modified process of interpretation must be developed in order that the imperfect but magnified image may be interpreted correctly.

TELESCOPIC SYSTEMS

While the precise type and power of the magnifying system which may be required can be determined only by actual trial in any given case, there are certain general principles which apply to most of these cases. Telescopic systems, for example, designed to fit into the usual practical limitations of space, rarely give more than a 2.2× magnification to the visual angle. Thus these appliances are useful only in the lesser grades of visual deficiency. Practically, they are used according to need in individuals whose best visual acuity with ordinary corrected lenses would fall between 20/50 and 20/400 on the Snellen chart. Occasionally, individuals with poorer vision may appreciate them.

It is impossible to decide, on the basis of ordinary refraction procedures and the visual acuity obtained by them, whether or not the telescopic or other magnifying device would be helpful in a given case. Only by trial can this be determined and therefore the ophthalmologist must have available a telescopic system so designed that it can be used for test purposes in a trial frame or phorometer. Figure 4 shows a 2.2× telescope, mounted in a trial case ring and in use in a phorometer. The actual procedure is simply that of placing the telescope in front of the already determined correction and noting the increase in the patient's visual ability, keeping in mind, that in all probability the ultimate visual improvement will be considerably more than is at first apparent.

It is often desirable to modify the lenses already in the trial frame or phorometer, as ofttimes, the lens correction has been uncertain because of the diminished visual ability, and the magnification introduced by the telescope permits a more accurate subjective lens correction. It is even possible to use a retinoscope for objective testing through the telescope. Fixation should, of course, be at the usual 6 meters if at all possible. If not, the test apparatus may be brought somewhat closer, and certainly so if the telescope is designed to be used for fixation at some point within the 6 meter distance.

If a perceptible improvement in vision results from the use of the telescope, the effect of near additions may be ascertained by attaching the additive lenses, several of which should be available in additions ranging from +3.00 D. to +12.00 D. The more powerful the addition, the closer the patient will have to hold the near point test object, so, if possible, a nice balance should be struck between the increased visual ability of the patient and the nearness of the test material. The addition should be the least powerful which would give the desired vision at the most remote point. Although there is considerable need for some training and judgment in the prescribing of these appliances, the procedure itself is relatively simple.

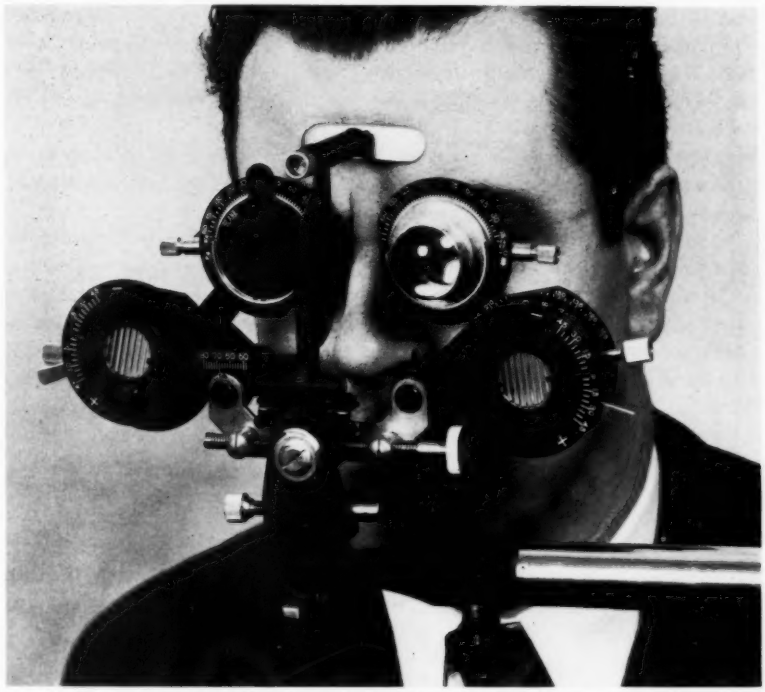


FIG. 4. 2.2× telescopic element mounted in trial ring and in use in a phorometer

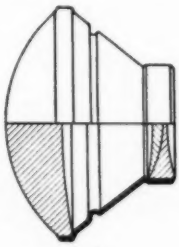
TYPES OF TELESCOPIC APPLIANCES

Telescopes to be used in connection with spectacles for individuals with deficient vision have been used for somewhat over a century. Pritchard, in 1850, and Steinheil, in 1866, introduced and perfected the "Stopsellinse" or "Steinheil conus". In 1911, the advance in the production of optical glass and the perfection of lens designing permitted Von Rohr to design a well corrected telescope of 2.2× with a fairly adequate field (Fig. 5). A whole series of these was designed for different refractive conditions, particularly myopia, but eventually only the plano telescopes were used extensively with attachable caps containing the patient's refractive lens correction next to the eye, and other and larger caps over the outer lenses with convex lens additions for near. At the present time, these are not obtainable in their original form and the commercial varieties are limited to those manufactured by the Kollmorgen Corporation and the Univis Lens Company. The Kollmorgen telescopes are similar to the Zeiss design and are basically 1.7× and 2.2× with additive caps for near vision ranging from +3.00 D. to +12.00 D. (Fig. 6).

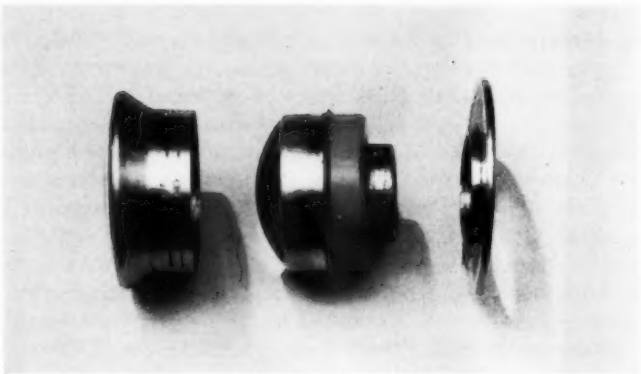
The Univis telescope is essentially a compound Steinheil cone, constructed as described earlier in this paper, and mounted in a spectacle lens, which is in-

serted in a suitable frame. This lens has the advantage, in common with that to be next described, of permitting the patient to walk around while wearing it. The Zeiss-Kollmorgen type does not permit the use of peripheral vision and consequently ambulation is difficult because of the displacement of objects in space by reason of magnification.

Some years ago, this writer designed a bifocal telescopic system in an open mount which permitted normal spatial judgment while, at the same time, providing telescopic magnification for both distance and near. Such an appliance can be made in any well equipped optical laboratory, although it will have to be designed by the ophthalmologist who must specify the lens curves to be used and the separation of the elements. Figure 7 illustrates the appearance of such an appliance and Figure 8 shows a typical optical system with the necessary curves when ordinary optical glass is used. The lens nearest the eye consists of a plano lens or a correction lens on which the cylinder, if any, is on the inside surface and on the outer aspect of the near lens are concave countersinks which, together with the concave near surface, provide the complete concave ocular



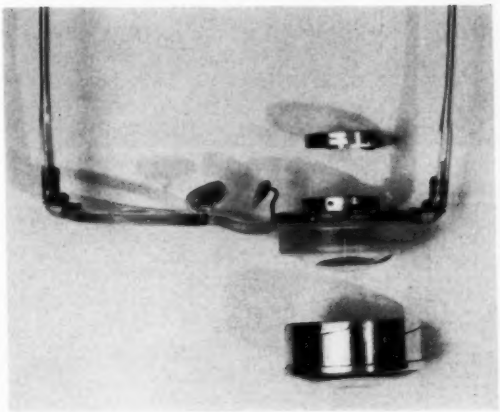
A



B

FIG. 5. The upper drawing is that of a Von Rohr (Zeiss) telescope in quarter section, to show construction. The lower illustration is that of a 2.2× Kollmorgen old type telescope adapted for use in a trial frame or phorometer. The outer cap is for the reading addition.

element of the telescope. The outer element is a plano lens with concentric surfaces and with two cemented wafers which provide, together with the outer surface of that lens, the necessary convex element required for distance or near fixation. The concave countersinks on the lens nearest the eye are difficult to



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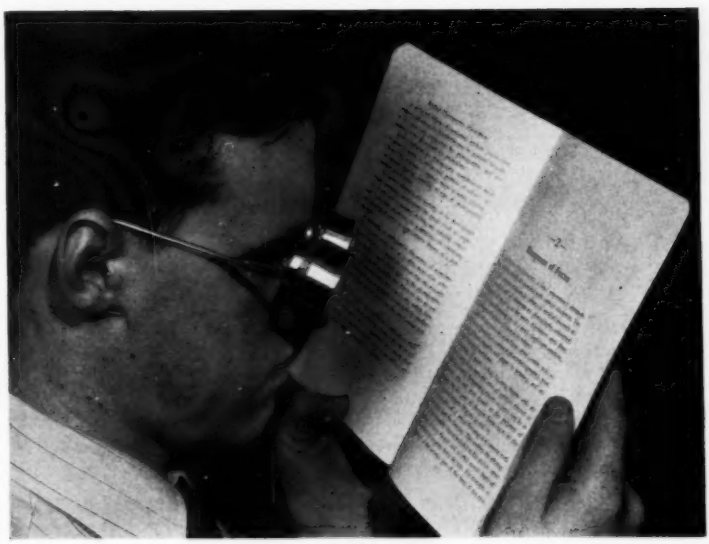


B

FIG. 6. Other types of telescopic magnifiers. *Upper.* 1.7× Kollmorgen telescope with small cap for the patient's lens correction, and large cap for reading addition. *Middle.* 1.7× telescope with reading addition in use. *Lower.* Two simple attachable telescopes, the solid one made by the Aloe Company and the open one by a optician on prescription.

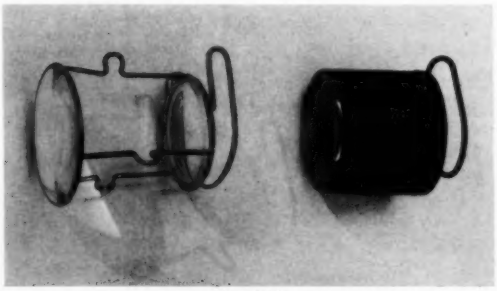


FIG 6C.

FIG. 7. Tait telescope in use, showing general design and construction

grind when they are much over −16.00 D., so generally they are about of that value.

In computing the curves for the usual plano telescope lenses, it is desirable to have the base curves of both nearly concentric with the somewhat shifting and indefinite "center" of rotation of the eyes. The latter is located approximately about 13 mm. behind the anterior corneal surface. If the vertex distance is then

designed to be 14 mm., the near surface of the lens next to the eye should be on a radius of about 25.5 mm., which would give about −20.00 D. This radius gives, however, too high a dioptric power, so that about 37.9 mm. (−14.00 D.) is usually used. This curve must be increased in the case of a concave lens basic prescription, or decreased if this is convex. If the base lens is a plano, then the outer curve should be designed to be concentric with it, which means slightly less in dioptric value.

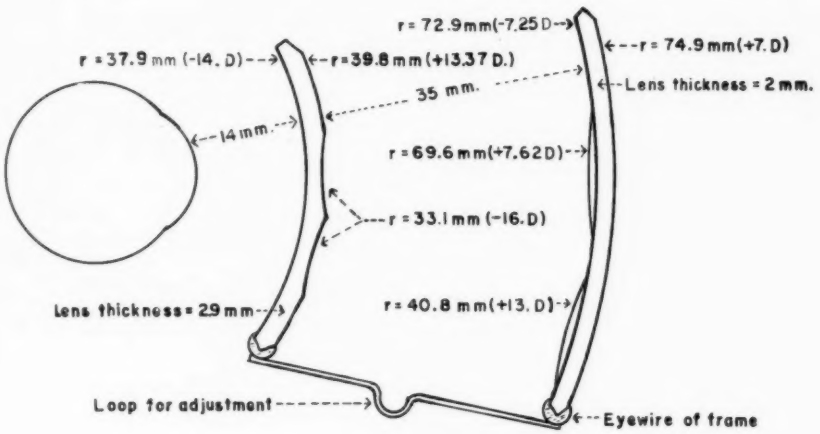
The usual distance between the near and outer lenses is 35 mm., which means that the curvature of the near surface of the outer lens has a radius of 72.9 mm., which gives a dioptric value of −7.25 D. The outer surface, to be concentric, would have a somewhat lesser dioptric value, actually about +7.00 D.

The dioptric value of these surfaces for any given radius of curvature is given by using the following formula:

$$D = \frac{n - 1}{r}$$

where D = Power in diopters
n = Refractive index
r = Radius in meters

With this basic setup, it is then necessary to make some "trial and error" computations in order to arrive at a satisfactory telescopic system. If it is


r = 72.9 mm (-7.25 D)
r = 37.9 mm (-14. D)
r = 39.8 mm (+13.37 D.)
r = 74.9 mm (+7. D)
35 mm.
Lens thickness = 2 mm.
14 mm.
r = 69.6 mm (+7.62 D)
r = 33.1 mm (-16. D)
Lens thickness = 2.9 mm
r = 40.8 mm (+13. D)
Loop for adjustment
Eyewire of frame

TAIT BIFOCAL TELESCOPE 2-X
Add −5.00 sph. for near
Cement wafers on outer lens = 18 mm. diameter
Countersinks on inner lens = 10 mm. diameter

FIG. 8. A typical Tait telescope of 2+× with detailed specifications of curves and distances of components.

assumed that the countersinks on the lens nearest the eye will be −16.00 D., with the curve on the other side −14.00 D., there would be a negative focal point for the combined power (−30.00 D.) of 3.33 cm. The power of the cement wafer added to the distance lens would then be such that its positive focus coincides with the negative focus of the countersink, in this case amounting to the negative focus of the countersink plus 3.5 cm. or 6.33 cm. These measurements would be for a "plano" telescope with no provision for the patient's ametropia except the add for near.

The magnifying power of the telescope will be the ratio of the two focal lengths, or slightly more than 2×.

If desired, adjustment for slight focal faults in the system may be provided for by small open loops in the three wires which are welded to the eyewires and which hold the lenses rigidly together. Opening the loops slightly will increase the distance between the lens elements and compressing them will shorten it. By sighting a distant object through the telescope and experimenting with extension and compression of the adjustment loop, a perfect focus may be attained.

SIMPLE MAGNIFYING SYSTEMS

This designation is somewhat misleading, as many simple magnifiers are actually made up of complex combinations of lenses, but they are so called to distinguish them from telescopic systems, which use convex object and concave ocular lenses. A simple magnifying system will consist either of a single convex lens or of two or three such lenses in juxtaposition.

The simplest type of magnifier is the familiar hand reading glass, which comes in a variety of forms and can be purchased not only in the optician's establishment, but in many other general and specialty stores in the average community. In general, these magnifiers vary in dioptric power from +4.00 D. to +40.00 D., and are ordinarily held in the hand or supported by legs or a stand at a distance from the printed page which is approximately equal to their focal length. Included in this general category are the "linen tester", a small folding magnifier designed for counting the threads in a given area of cloth, and the various types of loupes used by watch makers, physicians and others for small and delicate mechanical procedures and surgery (Fig. 9). Cylinder magnifiers, consisting of a section of a convex cylinder in a similar range of focal powers, and also supported on legs, are sometimes used where the visual acuity is only moderately reduced. This type of lens will increase the visual angle in the one direction only and consequently, if used correctly, will apparently increase the height of objects, leaving their width undisturbed.

Some of the simple magnifiers, particularly those mounted on a base or legs, are supplied with self-contained lighting systems, and for that reason are generally easier to use than the ordinary ones.

Simple hand magnifiers of these various types are generally used where the visual limitation is not excessive, such as individuals whose visual acuity is of the order of 20/100. A patient with bilateral immature cataracts, for instance,

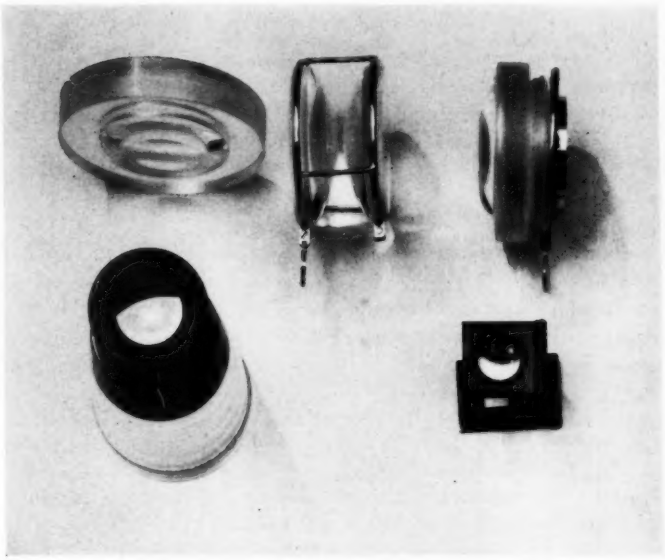


FIG. 9. Simple magnifiers. *Upper Left.* Convexo-concave doublet in plastic ring. 8×. *Upper Middle.* Plano-convex doublet in trial ring for use in phorometer or trial frame. 10×. *Upper Right.* Plano-convex doublet in plastic ring with adapter for trial frame or phorometer. 8×. *Lower Left.* Eastman magnifier with clear plastic bottom to provide light on object. About 4×. *Lower Right.* Linen Tester. These come in different sizes and focal lengths. The one shown is small with a $\frac{3}{4}''$ focal length. 12×. Larger ones provide less magnification down to 4×.

who still has about 20/100 vision in each eye with his normal correction lenses and who wants to do very little reading, may find it possible to read newspaper print with the hand or leg supported lens.

In this group of patients, as in those who will do well with telescopes, the appliances must be tried out in order to determine if improvement is possible. Even with the simple reading glass, a certain amount of practice, must ensue before the best possible results are obtained.

BIFOCALS AS MAGNIFIERS

It should be noted that the desirable effects of simple magnifying systems can often be obtained in this group of cases by prescribing sufficiently great bifocal additions. Bifocal additions, or their equivalent single lenses for reading, may be supplied up to +6.00 D. additions in the case of patients with binocular vision, or up to +10.00 D. or +12.00 D. additions where one eye only is used. This simple procedure should always be tried first before experimenting with the more complicated and more expensive appliances, provided that the vision obtained with them is adequate for the requirements of the patient.

DOUBLET MAGNIFIERS

Dioptric power in excess of +12.00 D. usually requires specially designed lenses to reduce the peripheral aberration which limits markedly the useful field. Such lenses must be designed as compounds consisting usually of two elements in juxtaposition and so calculated that the spherical aberration is reduced to a minimum, and such lenses are variously known as "compound magnifiers", "corrected magnifiers", "doublets" if made of two elements, or "microscopic lenses".

Figures 10A and 11 illustrate a simple and easily manufactured doublet, which has a sufficiently large field for such a powerful lens. This can be made in any optical laboratory where grinding equipment and frame welding apparatus are available. Because of the very close focal length of such lenses, they are for monocular use only. This is no hardship for the average patient who needs

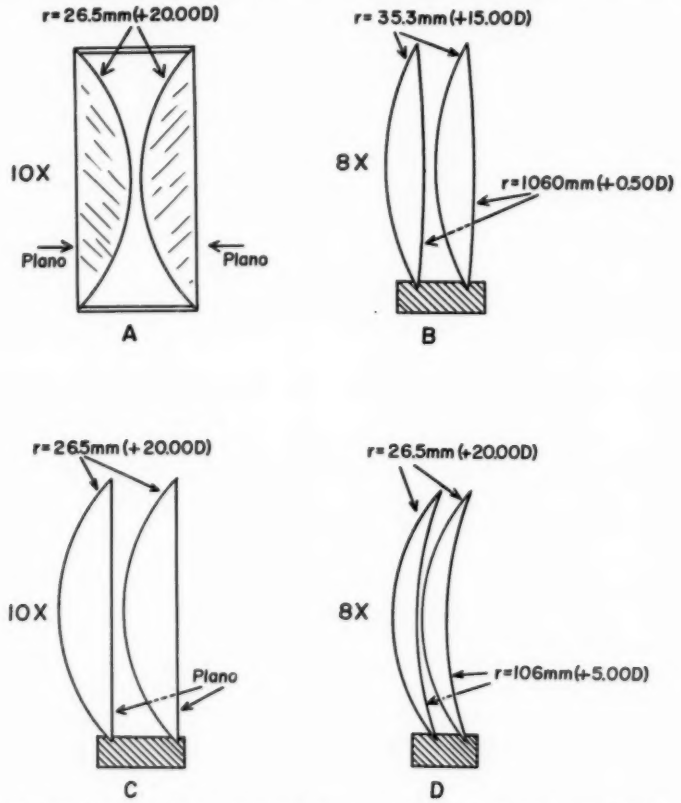


FIG. 10. Doublet magnifiers: Details of construction. A. Plano-convex doublet. 10×. B. Unsymmetrical biconvex doublet. 8×. C. Plano-convex doublet. 10×. D. Convexo concave doublet. 8×.

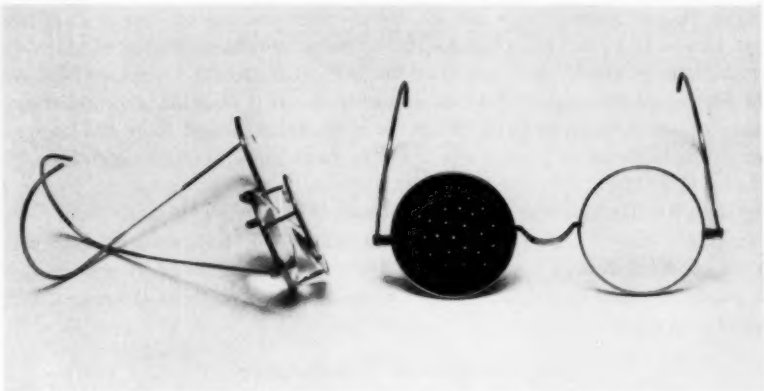


FIG. 11. Optical aids in severe visual disability. *Left.* Plano-convex doublet magnifier *Right.* Multiple pinhole spectacle

them, however, because practically all such individuals have one eye more useful than the other.

In the construction of these lenses, good results will be obtained if the outer surfaces are plano and the inner convex surfaces of equal strength.

Occasionally it is desirable, when the correction is complicated by high astigmatism, to incorporate a cylindrical curve on the ocular surface of the inner lens, and this can be done by the optician without difficulty.

It is also possible to design a doublet lens consisting of two convexo-concave or convexo-plano lenses with the convex surfaces facing outward. If properly designed, such lenses will give some measure of marginal correction and will be less bulky than the conventional plano-convex doublet, although not as simple to construct and generally not superior in practical use. Such lenses are also illustrated in Figure 10 (B, C and D).

Compound magnifiers of this type are of the greatest use to the patient with visual acuity of less than 20/100 in the better eye.

As with the telescopic appliances, the ophthalmologist should have available test lenses in trial rings, so that the result of using them in any case may be evaluated. Figure 9 shows a magnifier of this type so equipped. Magnifications of 8×, 10× and 12× are those which are most commonly used.

ASPHERIC MAGNIFIERS

It has been known for many years that a real correction for marginal aberration in high power lenses with large apertures can be obtained only by the employment of hyperbolic curves on the surfaces. Difficulties were experienced grinding such lenses using optical glass because the grinding process needs not only purely circular movement, but also a "to and fro" movement on the grinding tool, which could not be obtained with rigid tools with aspheric surfaces. Some twenty years ago Zeiss partially solved this problem by the use of slightly

flexible rubber forms which would permit some cross movements in grinding. Such lenses, however, although useful for astronomical instruments and certain precise lens systems, were not used to any great extent in ophthalmic work. The advent of transparent plastics, however, made it possible to produce hyperbolic surfaces with fairly good refractive characteristics and there has been some recent use of aspheric plastic lenses in the form of compound magnifiers. Such lenses will produce a larger field than spherical lenses of the same power, but they do have the disadvantage that the patient must look through them directly along their optical axes. Otherwise aberrations will be increased rather than decreased. This development is still in the experimental stage, however, so that for practical office use it is, for the present, better to depend upon spherical magnifying systems.

PROJECTION ENLARGEMENT

Enlargement of the visual angle by means of lens systems in front of the eyes is not the only method by which the visual angle can be increased. Any projection method and screen may be utilized for this purpose. The "movies" are a familiar example of the extent to which magnification may be obtained by a projection method. Utilizing the principle of the Baloptican, it is possible to project opaque material, such as the page of a book, and this method is utilized in the "Megascope" of the American Foundation for the Blind and the Franklin Institute device now being developed by the American Optical Company. The latter of these is of relatively low power and is useful in the lesser degrees of visual disability, while the Megascope will give considerably more magnification, although with a smaller field, and is thus better adapted for those with a greater visual deficiency. These instruments must be seen to be appreciated, and as they are expensive and will be relatively rarely used, it is unlikely that they will be part of the permanent office equipment of any ophthalmologist unless he sees many patients with severe visual disability. They will, however, be available for trial in many areas, and should be kept in mind as a possible solution for a visual problem in suitable cases.

1324 West Main Street *Norristown, Pennsylvania*

Clinical Practice

THE INTRAOCULAR PRESSURE

PATHOLOGY OF PRIMARY GLAUCOMA

E. Redslob

Ophthalmic Clinic of Strasbourg, France

Ann. d'Oculist., 1955, *188:* 781–826

In the evolution of primary glaucoma two different types of corneal edema may be observed. The first is transient and related to the increase of intraocular pressure which causes displacement of the corneal lamellae and interference with the refraction of light. The second arises because of interference with corneal metabolism and is localized within the epithelium and persists.

The canal of Schlemm is always patent if the angle is open and may remain patent even if there is an occlusion of the angle. The volume of the anterior chamber is not dependent upon the degree of filtration but is related to swelling of the ciliary body. Atrophy of the iris and ciliary body occurs frequently but nonetheless the ciliary body is edematous. Swelling of the vitreous is caused by variations in the pH with a resultant increase in intraocular pressure.

Hemorrhages occur frequently in the retina and cavities resembling those of Schnabel in the optic nerve may be present. Ganglion cells and visual cells are surprisingly little damaged.

Excavation of the optic nerve is due to arteriosclerosis at the disc where vessels are scarce, even in the normal eye. In the intervaginal space, veins are characteristically hyalinized and dilated. The optic atrophy is due to sclerosis of arteries and capillaries which causes an initial degeneration of nerve tissue. Eventually cavities develop and the entire nerve is invaded by scar tissue.

Comment: In this article Redslob summarized the findings in 56 globes which had suffered from chronic primary glaucoma, and 4 with acute glaucoma. His conclusions regarding the two types of corneal haze are certainly the generally-held view. However, his conclusions regarding the cause of the glaucoma bring up many debatable questions. As for the idea that it is not the degree of filtration but the pressure from behind the iris and ciliary body which decides the anterior chamber volume, one must immediately separate the cases clinically. If one speaks of the acute glaucoma cases, then we would agree that the swelling of the ciliary body is one factor which may force the iris against the trabeculum and prevent filtration, but this is still a filtration problem. There is no evidence that at the physiologic pH vitreous swelling is a factor. In simple glaucomatous eyes studied in vivo

gonioscopically and tonographically it is certainly proven that the chamber angle is open and filtration impeded beyond the entrance to the trabecular spaces.

Studies of enucleated globes which have suffered from the primary glaucomas tend to give a false impression of the pathogenesis of the diseases since such globes are usually removed long after the disease has begun and usually after unsuccessful surgical treatment.

Although the reviewer agrees with the concept of vascular changes being responsible for atrophy of the optic nerve at least in some cases, it is difficult to prove in the type of material here studied.

The pathogenesis of primary glaucoma will be determined from physiologic studies and not from the findings of globes enucleated long after the disease process has started. However, this should not detract from the facts which we can learn in relation to the clinical course of the disease from such studies.

H. Saul Sugar

SIX-YEAR EXPERIENCE WITH ELECTROLYTIC CAUTERIZATION OF LONG CILIARY ARTERY AND CILIARY BODY (CILO-CYCLO-ANOLYSIS)

H. Stumptner

Erlangen, Germany

Deutsc. Ophth. Gesellsc., *1953*, pp. 84–93.

Since 1947, when Schreck devised cilo-cyclo-anolysis as a new method of surgical intervention for glaucoma, 232 eyes have been operated on by this technique. A spatula shaped electrode coupled with the anode is introduced subsclerally four mm. from the limbus where the muscle ring of the ciliary body provides effective internal protection. The exact subscleral position of the electrode is controlled under direct vision: the electrode is pushed forward from an incision parallel to the limbus, meridionally into the angle of the chamber and then, by slowly dividing the angle of the chamber, its position is changed into one parallel to the limbus over the branches of the long ciliary artery and electrolysis is carried out. After-treatment consisted of topical administration of scopolamine for at least one week. Of 53 eyes with glaucoma simplex, 32 were regulated without the administration of miotics. "Regulated" means that the ocular pressure remained below 30 mm. Hg and that, under continued observation, the vision and the visual field did not show any decrease for which the glaucoma could have been held responsible. Eighteen eyes were regulated with the aid of miotics and the operation was not effective in three eyes. Of 55 eyes with chronic glaucoma, 24 were regulated without the administration of miotics, and 12 of these were regulated for more than three years. Twenty-three were regulated with the aid of miotics, and 4 of them for more than three years.

Eight eyes were not regulated, and one had to be enucleated. Of 40 eyes with inflammatory chronic glaucoma, 20 were regulated without the use of miotics, and 16 of these for more than three years. Thirteen eyes were regulated with the aid of miotics, and 7 of these eyes for more than three years. Seven eyes were not regulated, but three of these could be maintained free of pain, while one had to be enucleated.

Iridectomy remains the method of choice for acute inflammatory glaucoma; cilo-cyclo-analysis used as a second operation proved to be valuable in that the pressure could be regulated without miotics in three eyes, and in two of these for more than three years. The pressure was not reduced in three additional eyes. Of 13 eyes with hydrophthalmos, 7 remained regulated for more than three years, while cilo-cyclo-analysis failed in the remaining 6.

Cilo-cyclo-analysis proved effective in some types of secondary glaucoma. In cases of leukoma adherens, combined treatment with cilo-cyclo-analysis and loosening of extensive anterior synechiae was practiced. Of 20 eyes operated on according to this technique, the pressure was regulated in 11 without the use of miotics, in 6 eyes regulation was maintained for more than three years with the use of miotics, and in 3 eyes results were not satisfactory. Only 3 of 15 eyes with luxated lens remained unimproved, 5 were regulated without miotics and 7 with miotics. Good results were obtained with cilio-cyclo-analysis in six eyes with aphakic glaucoma. Only three cases of secondary glaucoma after an occlusion of the central retinal vein (so-called thrombosis) were therapeutic failures. With regard to lowering of pressure in glaucoma simplex, comparison of results obtained with cilo-cyclo-analysis and with Elliot's method of trephining was favorable. Cilo-cyclo-analysis offers four advantages as compared to trephining: (1) no late infections because no opening remains in the sclero-cornea; (2) no postoperative losses in the central visual field; (3) the anterior chamber is not lost; (4) profound and prolonged hypotomy does not occur. In cases of inflammatory chronic glaucoma 50 per cent of the eyes subjected to cilo-cyclo-analysis were regulated without the use of miotics, as compared to 24 per cent subjected to Elliot's trephining, and 14 per cent after iridectomy and cyclodialysis.

Therapeutic failures occurred in 17 per cent of the cases in which cilo-cyclo-analysis was used, in 26 per cent of trephining, and in 32 per cent and 48 per cent after iridectomy and cyclodialysis, respectively. Results of cilo-cyclo-analysis in absolute glaucoma were comparable to those of Elliot's trephining. In aphakic glaucoma the results obtained with cilo-cyclo-analysis was better than those obtained with the classic cyclodialysis. Cilo-cyclo-analysis is the method of choice for those types of secondary glaucoma in which indurations of the iris, lens, or vitreous body block the angle of the anterior chamber. Cilio-cyclo-analysis has one disadvantage which consists of hemorrhages which rarely occur immediately or within several days after the operation. They may be prevented by repeated paracentesis with injection of air into the anterior chamber. In cases of definitely hemorrhagic glaucoma the author prefers Vogt's cyclodiathermy puncture to cilo-cyclo-analysis.

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Comment: Stumptner's work is important in that it gives the results of a considerable number of operations aimed at lowering the intraocular pressure through diminution of the blood supply to the ciliary body, with subsequent decrease in the rate of formation of aqueous humor. Several techniques have been used by other authors including diathermy to the region of the long posterior ciliary arteries through the conjunctiva (Arruga and Scheie, Frayer and Spencer) and directly to the sclera after detaching the medial and lateral recti (Acto-Peis). Schreck (1949) first introduced the cilo-cyclo-anolysis operation. An incision was made 2 mm. behind the insertion of the medial or lateral rectus muscle or both and a cyclodialysis spatula inserted parallel with the limbus at right angles to the course of the long ciliary arteries. A current of 5 ma. was applied to the spatula for 5 seconds as a cyclodialysis was accomplished. Stumptner applied his coagulations in an area 7–8 mm. from the limbus and extending 4–5 mm. above and below.

The purpose of the cyclodialysis in this operation is unrelated to its ordinary purpose. Here is a simple means of direct application of the coagulating current to the long ciliary artery.

H. Saul Sugar

EXPERIMENTAL ASPECTS OF NERVOUS CONTROL OF THE OCULAR CIRCULATION AND INTRAOCULAR PRESSURE

E. S. Perkins

London, England

Acta XVII Concilium Ophth., 1954, 1157–1163

Experiments have been performed on animals, chiefly albino rabbits, to determine the effect produced on episcleral and choroidal vessels and intraocular pressure by dividing and stimulating the cervical sympathetic nerve and the third cranial nerve, and by stimulating the seventh and fifth cranial nerves. In some experiments, the temperature in the region of the ciliary body was also measured by means of a small thermocouple inserted through the sclera. If the external conditions remain constant or are compensated by another thermocouple, changes in temperature reflect changes in blood flow in this region. A rise in temperature indicates an increased flow and vice versa.

Cutting the cervical sympathetic nerve in the rabbit was followed by vasodilatation of the skin vessels and slight vasodilatation of the episcleral vessels on the side of the divided nerve, though no changes were observed in the choroidal vessels. The intraocular pressure was little changed, but a rise in the temperature of the ciliary body has been recorded, indicating some increased blood flow in the ciliary region.

Stimulation of the cervical sympathetic was followed by marked changes in the episcleral vessels. The whole limbal region became avascular and previously observed aqueous veins could not be distinguished. With a smaller stimulus, however, there appeared to be an increase in the aqueous outflow associated with

a decrease in the caliber of the blood vessels. When Evan's blue was injected into the anterior chamber, a blue stream of aqueous could be observed to flow freely in the aqueous veins even with a strength of stimulus which caused blanching of the blood vessels. Observations on the choroidal system failed to reveal any pronounced change in caliber of the larger vessels during sympathetic stimulation, although some lightening in color of the choriocapillaris suggested vasoconstriction of these small vessels.

The intraocular pressure always fell during sympathetic stimulation and temperature recordings indicated a decrease in blood flow through the ciliary region. It is apparent therefore that the sympathetic nervous system is able to regulate the blood flow in the ocular vessels and can cause a definite vasoconstriction.

Only the effect on intraocular pressure and blood pressure was studied in the experiments on the third cranial nerve. Since the parasympathetic outflow to the eye runs in this nerve, it was hoped that some evidence of vasodilator fibers might be found. Cutting the third cranial nerve in rabbits had no effect on intraocular pressure or blood pressure, but stimulation of the nerve produced a rise in intraocular pressure due to contraction of the extraocular muscles. When this contraction was abolished by decamethonium iodide, stimulation caused no change in intraocular pressure, though constriction of the pupil showed that the parasympathetic supply to the iris was being stimulated. It was evident, therefore, that no vasomotor effect sufficiently marked to cause any change in intraocular pressure was produced.

Other investigators have shown that vasodilator fibers supplying the cerebral vessels run in the seventh cranial nerve, leaving it at the geniculate ganglion. Experiments to see if these fibers also supply the eye were performed on rhesus monkeys from which the cervical sympathetic nerve, stellate and upper cervical ganglion of one side had been removed some six weeks previously. Electrical stimulation of the seventh cranial nerve through an enlarged trephine opening produced no significant changes in intraocular pressure when facial muscle contractions and roving eye movements were suppressed by the intravenous administration of decamethonium iodide. No temperature changes were found when the experiments were repeated with a thermocouple inserted through the sclera adjacent to the ciliary body. It may reasonably be assumed therefore that no vasomotor fibers reach the eye from the seventh cranial nerve.

Electrical stimulation of the fifth cranial nerve had little effect on intraocular pressure; mechanical stimulation, however, produced a decided rise in the intraocular pressure on the side stimulated, and in a few cases a contralateral rise in the pressure occurred after an interval of 15 to 20 minutes. Vasodilatation with an increase in blood flow and an increase in the permeability of the intraocular capillaries also followed mechanical stimulation of the fifth cranial nerve. It should be noted that all the stimulations of the fifth nerve were performed with the nerve intact, because there is at present no satisfactory method of dividing the nerve without causing stimulation and so affecting the blood vessels and the intraocular pressure.

These findings show that in the animals studied, the sympathetic system and

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the sensory supply to the eye are both capable of modifying the ocular circulation and causing a change in intraocular pressure. Changes of this character were produced by the experiments on both the cervical sympathetic and the fifth cranial nerves, but not by those on the third and the seventh cranial nerves.

Comment: This paper is part of a recent trend of experimental studies to investigate the nervous control of the intraocular pressure and the ocular circulation. Perkins' findings suggest that a central mechanism controls the intraocular pressure and that a central mechanism exists which affects the controlateral eye.

We have ample evidence for the diencephalic control of retinal blood vessels and of other vessels of the eye. Through the effect on these vessels we can expect changes in the rate of aqueous formation to result and thus effect changes in the intraocular pressure. However, the experiments suggest more direct effects on the intraocular pressure, perhaps through an effect on the resistance to aqueous outflow. Further experimental work must demonstrate this.

The effect on the contralateral eye has been known to some extent clinically. Experimental evidence that more is involved than vascular reflexes remains to be demonstrated.

H. Saul Sugar

TREATMENT OF OCULAR HYPERTENSION BY ADRENALIN AND DIVERSE SYMPATHOMIMETIC AMINES

R. Weekers, Y. Delmarcelle and J. Gustin

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Am. J. Ophth., 1955, *40:* 666–672

The instillation of two per cent adrenalin into the eye induces a reduction in tension in glaucoma simplex, an action which has been attributed to the reduction of the rate of aqueous formation. The rapidity of disappearance of fluorescein from the anterior chamber was measured in a series of normal patients and patients with glaucoma following the instillation into the eye of two per cent *l*-adrenalin. The study indicated that there was a lasting diminution of aqueous production and that the tension lowering action was due to this and not to improvement of drainage conditions. Drugs without appreciable sympathomimetic activity like *d*-adrenalin and adrenalone were without a tension-reducing effect. The reduced tension thus apparently results from sympathetic stimulation.

The hypothesis that the reduction of the formation of aqueous is determined by vasoconstriction and the lessened blood flow in the ciliary body that follows should be abandoned. The reduction in tension after the instillation of *l*-adrenalin is much more prolonged than the vasoconstriction visible in the conjunctiva; moreover aleudrine, which is not a vasoconstrictor, possesses like *l*-adrenalin the same property of lowering ocular tension. A plausible hypothesis according

to which *l*-adrenalin and aleudrine alter the metabolic processes required for the formation of aqueous is suggested.

Comment: Weekers and his co-workers present indirect evidence from fluorometric measurements that adrenalin and sympathomimetic amines reduce the formation of intraocular fluid. The mechanism by which sympathomimetic amines such as adrenalin reduce intraocular pressure has not been firmly established. It is suggested here that they are effective not because of their vasoconstricting action, but through some other mechanism. They suggest that these agents might interfere with metabolic processes required for the formation of aqueous. It must be realized that these are indirect observations; that the circulation directly to the ciliary body was not studied. It is true that the vasoconstriction produced by these agents is not of long duration and Dr. Weekers and his coworkers have stressed that aleudrine produces no vasoconstriction but does lower intraocular pressure. Such a study points out the necessity for developing a method of accurately measuring the blood flow through the ciliary body as influenced by these agents. The ascorbic acid method of Linner and Becker might help in such a study.

IRVING H. LEOPOLD

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INJURIES

THE EXTRACTION OF INTRA-OCULAR FOREIGN PARTICLES OF A NONFERROUS METALLIC NATURE: PRELIMINARY EXPERIMENTS WITH A NEW ELECTRONIC MAGNET

JOHN HARRY KING, JR., WILLIAM VAIL LOVELL, ALFRED A. J. DEN, M. NOEL STOW AND WILLIAM C. OWENS

Washington, D. C.

Acta XVII Concilium Ophth., 1954, 549–557

About 25 per cent of all intraocular metallic foreign particles found in injuries incurred in the Korean conflict were non-magnetic. Therefore, efforts have been made to develop an electronic metamagnet capable of attracting non-magnetic metals.

The ocular metamagnet is a modification of the electromagnet. Its circular, tapered head consists of two, water cooled, copper coils. The central, "attractor coil," is surrounded by a "field coil." This head is supplied by an amplifier of 25 kilowatt capacity in frequency ranges of 5,000 to 10,000 cycles per second. A variable frequency oscillator impresses the requisite frequency on a pre-amplifier which supplies the 500 watt amplifier. This in turn gives energy to the grids of six power tubes. The output of the power tubes is stepped down in two stages to reach the magnet at a voltage low enough to be suitable for operating room usage. The power tubes are cooled by forced air.

With this metamagnet 1 to 2 mm. of aluminum or copper can be attracted 10 mm. through a viscous medium. Brass, lead, monel metal, and certain stainless steels are more difficult to attract. Lead shot 4 mm. in size can be drawn about 6 mm.

Preliminary experiments have been performed with foreign particles of aluminum, copper, magnesium and brass implanted in cat eyes. Particles implanted from several hours to three days before operation, could be drawn to a corneal or scleral incision and extracted. However, if a period of 10 to 14 days had elapsed after implantation, a fibrinous inflammatory exudate firmly held the particle, preventing its removal. In the cat eye no pathologic effects have been noted as a result of exposure to the high frequency current.

Human experimentation has not been performed as yet, since further research and development are necessary to increase the power of the metamagnet before its application to clinical ophthalmology can be tested.

Comment: This article reports the results of an investigation of one of the most important phases of intra-ocular foreign body surgery: the problem dealing with non-ferromagnetic intra-ocular foreign bodies. The inability of the surgeon to remove this type of foreign body without severe damage to the eye led to many enucleations. It is regrettable that the group and the government have appeared to discontinue their research in this important field.

GEORGE M. HAIK

The recent resurgence of epidemic keratoconjunctivitis in several parts of the world made it advisable to restudy the whole problem of the etiology of this eye infection. Attempts were therefore made to isolate viruses from the eye and to investigate the formation of neutralizing antibodies in patients with epidemic keratoconjunctivitis and herpetic keratitis. The result was the successful isolation of a new virus belonging serologically to the group of APC viruses and classified as type 8 from a patient with clinically typical epidemic keratoconjunctivitis. Serologic investigations showed that 25 persons who also had typical epidemic keratoconjunctivitis had neutralizing antibodies to this new virus (named Trim after the first patient from whom it was obtained). The patients, in 19 of whom the antibodies were present in serum dilutions of 1:20 or greater, came from four distinct geographic areas in North America (Canada, Philadelphia, Pacific-California, and Chicago). Similar antibodies were found in only one of 19 patients with herpetic keratitis and in only one of 10 with uveitis. Typical herpes-simplex virus was isolated from a patient during the acute phase of epidemic keratoconjunctivitis while she was undergoing infection with the APC-like agent, as shown by a rise in antibody titer. It seems at least possible, therefore, that APC agents, such as Trim virus, may be an important factor in causing epidemic keratoconjunctivitis, but that they may require another agent, such as herpes virus or trauma, to produce the full-blown clinical picture. Whatever the exact nature of the relationship between Trim virus and epidemic keratoconjunctivitis, its existence seems to be clearly established by the evidence presented. E. Jawetz, S. J. Kimura, L. Hanna, V. R. Coleman, P. Thygeson, and A. Nicholas, the Departments of Microbiology, Ophthalmology, and the Francis I. Proctor Foundation for Research in Ophthalmology, University of California Medical Center, San Francisco, California, Am. J. Ophth., 1955, 40: 200–211.

THE ORBIT

ORBITAL DECOMPRESSION IN ASEPTIC CAVERNOUS SINUS THROMBOSIS

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Acta XVII Concilium Ophth., 1954, 250–256

Cavernous sinus thrombosis, septic or aseptic, formerly had a very high mortality. Chemotherapy and anticoagulants have markedly diminished the mortality, but the ocular sequelae continue to present a serious therapeutic problem. Several authors have reported that incomplete recovery of the ocular functions, optic atrophy, ptosis, and external ophthalmoplegia are often the permanent results of venous obstruction and of prolonged orbital pressure. Combined treatment with anticoagulants to arrest the thrombosis and bilateral orbital decompression to reduce edema and relieve the pressure on the optic and other cranial nerves successfully prevented permanent ocular damage in a patient with aseptic cavernous sinus thrombosis following a moderate head injury.

The patient, a 45-year-old woman, struck the left temporal area of her head on the floor of a swimming pool 10 days before she was first seen. The day after the injury she had pain over the left ear and in the region of the left mastoid. Gradually, pain developed in the left ear, on the entire left side of the head, and behind the left eye. Tinnitus became severe. Diplopia and ptosis began three days before the first examination. The findings were as follows: moderate tenderness over the left mastoid, temple and in the area of the origin of the internal jugular vein; complete ptosis of the left upper lid; complete external ophthalmoplegia. The left globe was markedly proptosed and there was conjunctival chemosis. The pupil reacted normally and the fundus of the left eye was essentially negative, but the vision was 20/200. The right eye had a small subconjunctival hemorrhage, slight edema of the upper lid, and slight limitation of vertical movement. The vision in the right eye was 20/25. It was assumed that the injury to the left temporal area of the skull had damaged the lateral sinus, and that the resultant thrombosis had spread downward to the jugular bulb and anteriorly to the left cavernous sinus, and that it was progressing to the right cavernous sinus. The patient was admitted to the hospital and treatment was started with anticoagulants (heparin and the coumarin compound, Dicumarol).

Progress was satisfactory subjectively. The intense pain subsided, the tinnitus ceased, and the patient felt better. She was discharged from the hospital 10 days after admission, because it was felt that further anticoagulant therapy was dangerous and unnecessary inasmuch as the progress of the thrombosis had

stopped and there was no evidence of infection. The patient's external appearance, however, remained unimproved.

Nine days after discharge from the hospital, the condition of the patient's eyes was much worse. The conjunctival prolapse was very severe and it was obvious that the right eye was also becoming worse as a result of the venous obstruction: it was losing vision rapidly and was beginning to show external ophthalmoplegia. Roentgenograms showed "erosion of the supra-orbital fissure on the left and in the middle third of the roof of the orbit, involving about 2 cm. of bone." The opinion of the roentgenologist was that there was pressure erosion. In view of these facts, it was felt that intraorbital pressure from the edema caused by the venous obstruction was undoubtedly going to result in permanent damage to both eyes unless some type of orbital decompression was carried out. The patient was therefore admitted to the hospital for the second time 10 days after her first discharge, and on the following day a bilateral orbital decompression was performed. The Berke modification of the Kronlein operation was used. A canthotomy was carried out first, and the incision was extended posteriorly. A large portion of the lateral wall of each orbit was removed and the lids were sutured over two pieces of plastic tubing. The postoperative period was uneventful. Improvement was rapid and the patient was discharged on the 12th postoperative day. Within six weeks, the vision was correctable to 20/20 in each eye, the visual fields were normal, there was no residual heterophoria, and no ptosis.

Undoubtedly, the favorable result in this case was due to the bilateral orbital decompression. The use of chemotherapy, anticoagulants, and cortisone was not sufficient, as was proved by the course of the disease. The decompression permitted reduction of orbital edema and relieved the pressure on the optic nerve and other cranial nerves. The fact that there was roentgenologic evidence of pressure erosion indicates that the damage was caused by pressure and that decompression was effective because it immediately relieved the pressure.

Orbital decompression is therefore recommended in cavernous sinus thrombosis after the thrombosis has been arrested, since venous obstruction at this time often results in gross ocular damage. If a septic process is present, antibiotics as well as anticoagulants will of course be necessary.

Comment: This case report is of interest from the standpoint of calling our attention to an infrequent but serious intracranial complication of a casual head injury. In the average situation involving trauma to the head, little importance is attached to the injury unless a fracture can be demonstrated or symptoms of headache and mental confusion develop within the 48-hour period after injury. In the case of aseptic cavernous sinus thrombosis, however, the symptoms may not develop until a period of one week has passed from the time of injury. This delay is due to the very slow and insidious formation of the clot within the cavernous sinus. Therefore, by the time the symptoms of venous obstruction appear the patient may have forgotten about the injury.

This complication of head injury is a serious one because of the serious sequelae (ophthalmoplegia, proptosis, and loss of vision in the affected eye) that may develop. Although the author's case had a successful recovery, the majority of case studies, published

prior to this report quite a different outcome. So serious is the complication that those of us who have had experience with similar cases, particularly those of the septic type, prior to the discovery of antibiotics considered it fortunate if the patient survived.

With the widespread use of the chemotherapeutic agents and antibiotics in the past 15 years the septic sources of cavernous sinus thrombosis have been nearly eliminated, so that this disorder is much less frequent. So seldom is a case of either aseptic or septic cavernous sinus thrombosis encountered that some ophthalmologists pass through their two or three year period of graduate study without observing a single case. Likewise, a case report of cavernous sinus thrombosis is so seldom encountered by the reading ophthalmologist that he is prone to forget the possibility of this disorder when considering the differential diagnosis of orbital edema associated with venous obstruction, proptosis, and ophthalmoplegia.

In the author's case anticoagulant agents were used during the initial phases of the disorder. The anticoagulant drugs, with or without antibiotics, have been a factor in the more successful outcome of other cases of cavernous sinus thrombosis of the aspectic type and this editor considers them a very useful adjunct to present-day therapies.

In the case under discussion the author attributes a great deal of credit for the successful outcome to the orbital decompression that was performed. During the initial 10 days of treatment, however, anticoagulants were used and the author pointed out that there was subjective improvement. At this point the anticoagulants were discontinued, "as it was felt that further anticoagulant therapy was dangerous and unnecessary since the progress of the thrombosis had stopped and there was no evidence of infection."

In view of the subsequent events (within two days after stopping the anticoagulants the orbital symptoms became much worse) it is difficult to understand upon what basis the author considered the progress of the thrombosis arrested and the anticoagulants to be unnecessary. Furthermore, the administration of anticoagulants on an ambulatory basis with reasonable supervision of the prothrombin levels is now done by many internists without undue danger to the patient. In short it is felt that had the anticoagulants been given a further trial the orbital surgery might have been deferred.

The basis upon which the orbital decompression was undertaken is another point to be discussed. As one of the indications for surgery, the author cited the findings on roentgenography of the orbit. These roentgenograms, taken within 17 days of the onset of symptoms, showed "erosion of the supra-orbital fissure on the left and in the middle third of the roof of the orbit, involving about 2 cm. of bone." It seemed unlikely that the mere presence of an edema in this orbit of approximately two weeks' duration would produce a pressure erosion involving a 2 cm. area of the roof of the orbit. If a pressure erosion were actually produced in so short an interval of time, it would more likely be produced by a mass of considerable substance.

"Erosion of the supra-orbital fissure" is also considered an unreliable indication of pressure in the orbit. In the normal skull there is usually considerable asymmetry in the superior orbital fissures and the inferior borders of these fissures are prone to be rather indistinct in many roentgenograms. The superior orbital fissure may look decalcified and eroded when it really is not.

The important feature of this case, however, is not what methods of treatment might have been used but the fact that there was such a full recovery with the treatment methods employed by the author. It was pleasant to read that the decompression was performed through the lateral route. Because of improved surgical techniques, this approach to the orbit is becoming more popular and may some day nearly replace the transfrontal ap-

proach that has been so widely publicized in the past 20 years. The author stated that he had removed "a large portion of the lateral wall of each orbit." For the benefit of those readers who might wish to try this operation for similar cases requiring decompression it would be of interest to know more details of the author's surgery and, in particular, how large a portion of the orbit was removed. In this way the author's successful result might more easily be duplicated by others.

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THE TREATMENT OF EXPANDING LESIONS OF THE ORBIT WITH PARTICULAR REGARD TO THOSE ARISING IN THE LACRIMAL GLAND

The Seventh Arthur J. Bedell Lecture

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Am. J. Ophth., 1956, *41:* 3–11

Expanding lesions of the orbit, and particularly those arising in the lacrimal gland, are more poorly treated than any of the other conditions encountered in ophthalmology. More than 90 per cent of the primary tumors and tumor-like lesions of the orbit seen at the Eye Institute have fallen into the following classifications (given in the order of their frequency): hemangioma, lymphomatous tumors (lymphoma, lymphosarcoma), chronic granuloma (pseudotumor), dermoid cyst, epithelial tumors of the lacrimal gland, peripheral nerve tumors (neurofibroma, neurilemoma), meningioma, and astrocytoma (glioma). Examination of this list shows that the treatment of these tumors will depend entirely upon their diagnosis.

Hemangiomas are well encapsulated, lie in loose areolar tissue, and can be actually shelled out by blunt dissection. A peculiar fact, and one that is hard to explain, is that these lesions have no apparent afferent vessel, so that they can be removed entirely without hemorrhage. Lymphomatous tumors are poorly demarcated, non-encapsulated, and friable. Surgical removal of these tumors is not necessary, because they respond exceptionally well to irradiation of the orbit. In the case of chronic granulomas, or so-called pseudotumors, surgical treatment is indicated only in so far as tissue is needed to establish the diagnosis. Removal of tissue for biopsy, however, is not entirely without hazard because the lesion is often quite vascular and hemorrhage may occur. After the diagnosis has been made, irradiation may prove effective, especially if the lymphocytic element predominates.

Dermoid cysts, when superficially located, can be excised by an incision through the skin directly over the lesion. Those that are deeper must either be removed by the Krönlein procedure or, if they extend into the cranial vault, must be treated by a neurosurgeon. Tumors of the peripheral nerves are of two kinds: neurilemomas and neurofibromas. Neurilemomas are characteristically well encapsulated and can easily be removed by the Krönlein procedure; orbital neurofibromas, on the other hand, because they usually invade the contiguous bone and often reach the cranial cavity and other vital areas, should be dealt with by exenteration as soon as possible.

Meningiomas grow so slowly, occasionally taking 20 or 30 years to reach an appreciable size, that temporizing is sometimes justified. When operation is required, a neurosurgical procedure is usually necessary because the primary site of these tumors is in the cranial cavity in most cases. Astrocytomas or gliomas of the optic nerve can be removed very satisfactorily by the Krönlein procedure.

Patients with primary expanding lesions of the orbit may present themselves to the ophthalmologist with exophthalmos with a palpable mass, or with exophthalmos but no palpable mass. The most important thing to remember in dealing with orbital lesions is that the appropriate treatment cannot be decided on until the diagnosis has been established. The sole exception to this rule is found in the case of a well localized, encapsulated lesion that can be satisfactorily removed by an operation.

Expanding lesions of the lacrimal gland present a special problem in treatment. Analysis of 113 cases of lacrimal gland tumors showed 35 granulomas, 27 carcinomas, 25 mixed tumors, 24 lymphosarcomas, and 2 adenomas. Clinically, all of these lesions are manifested as a well-demarcated, localized, firm mass palpable through the upper lid in the region of the lacrimal gland. They are closely associated with the contiguous bone and it is sometimes difficult to palpate the demarcation between the orbital margin and the lesion. Biopsy is essential for a correct diagnosis. From the figures given, it can be seen that about one third of the expanding lesions in the lacrimal gland fossa are not neoplastic and that about 30 per cent of those that are neoplastic (i.e., the lymphosarcomas) do not require surgical treatment. The lesions requiring surgical removal constitute about one half of all lacrimal gland tumors. From the cytological point of view, only about half of these are malignant.

Although it is apparently an incontestable fact that tumors of the salivary gland are comparable to those seen in the lacrimal gland, the cure rates for tumors in these two sites differ strikingly. The prognosis of salivary gland tumors is good and that of lacrimal gland tumors is extremely poor. Whereas Foote and Frazell found that from 25 to 30 per cent of their patients with salivary gland carcinoma followed for five years or more had no recurrence, only one out of all the patients with lacrimal gland carcinoma followed for five years or more in several series combined was living, and he had signs of recurrence. Obviously, therefore, the treatment of patients with lacrimal gland tumors leaves much to be desired.

Failure to treat epithelial tumors of the lacrimal gland effectively seems to be due chiefly to (1) ignorance of the correct diagnosis at the time treatment is started; (2) lack of attention to certain characteristics of these tumors, namely,

their tendencies to extend beyond their capsules, to seed, to invade bone, and to extend along nerves; and (3) an inadequate surgical approach. The great importance of accurate diagnosis in these, as in other expanding lesions of the orbit, may be seen when it is considered that if the tumor is mixed, local excision is indicated; if it is a carcinoma, exenteration must be performed; if it is a lymphosarcoma, it may be treated by irradiation; and if it is a chronic granuloma, temporizing is permissible because regression may occur spontaneously.

Comment: In this seventh Arthur J. Bedell lecture Dr. Reese has brought to our attention some of his views relative to the management of expanding lesions of the orbit. In particular he is concerned with the surgical handling of the neoplasms of the lacrimal gland. When an ophthalmologist such as Dr. Reese so aptly correlates his surgical experiences with the pathologic examination of the excised tissue, it is well to sit up and pay attention to his conclusions.

In the first portion of his lecture he concisely classifies the more common lesions of the orbit and briefly details their proper treatment. However, it is that portion of the lecture devoted to the neoplasms of the lacrimal gland that conveys his main theme, i.e., some revision in our surgical approach to these lesions should be considered.

In reviewing his analysis of 113 cases relative to the incidence of the various neoplasms affecting the lacrimal gland it was a surprise to this reader to find that approximately one-third of the total were "granulomas," as he uses the term. Although I have not scrutinized a similar survey of lacrimal gland tumors from my own files, it has always been my clinical impression that the serious neoplasms rather than the relative benign "granulomas" were in the vast majority so far as those requiring surgical management.

In the terminology of the neoplasms of the lacrimal gland the author takes cognizance of the gradual change that has come about in the nomenclature of "mixed tumors." At one time practically all neoplasms of the lacrimal gland could be classified, pathologically, as mixed tumors. But with time it was found that some mixed tumors were much more malignant than others. This brought about some revision in the practical classification of these tumors so that those of malignant trend with predominant epithelial components were listed simply as varieties of carcinomas. Although such differentiation from a strictly histologic viewpoint is not ideal, it does allow a more practical evaluation of these tumors, particularly from the standpoint of their prognosis and proper treatment.

Dr. Reese reserves the term "mixed tumor" for the more benign-appearing neoplasms that usually possess some degree of encapsulation. He defines the term nicely by referring to these tumors as possessing a "benign cytology but malignant behavior based on the fact that seeding may occur." The term, seeding, is used in the sense that implants of the neoplasm can occur in the surrounding structures if the contents of the neoplasm get beyond the confines of its capsule either during the process of natural expansion or through an accident in its removal.

In one of the earlier paragraphs of his lecture Dr. Reese points out the need for making a correct diagnosis of the orbital mass so that the rational treatment can be applied. He repeats this phrase of wisdom several times during the paper and stresses the need for biopsy. He further points out that "those who are well versed in cancer work feel that the removal of tissue for biopsy does not jeopardize the prognosis." In respect to this dictum I would voice some caution as it applies to the group of mixed tumors with which the author is so concerned. It is the act of biopsy prior to the removal of the mixed tumor, I believe, that contributes to their seeding and the complications that Dr. Reese so earnestly wishes to avoid.

Perhaps because I so infrequently encounter the innocent granuloma (an experience contrary to the author's as noted above) I regard all masses in the region of the lacrimal gland as possessing potential malignancy until proven otherwise. For this reason my prime concern is to perform as wide an excision as possible and then examine the histology of the specimen. In this way accidental breaks in the thin capsule of many of the mixed tumors can be minimized and the treacherous "seeding" avoided. The microscopic study of the tumor after it is removed then serves as a guide to a treatment program similar to the one outlined by Dr. Reese as the result of his biopsy studies.

In the complete text of this paper two photographs were included which showed bone invasion by a benign mixed tumor of a resected portion of the bony lacrimal gland fossa. It was not clear to me how the author differentiated such bone invasion from simple pressure erosion.

As regards the author's suggestion that a more radical surgical approach to epithelial tumors of the lacrimal gland be considered, I agree that our past concepts have proven very inadequate when we consider that the five-year survival rate is practically nil. The author's proposal that a complete exenteration be combined with a radical removal of the bony orbit around the area of the lacrimal fossa seems a step in the right direction. In my own small series of patients that have undergone this radical operation the period of follow-up observation has been too short to determine the survival rate. A period of five to ten years will have to elapse before we can determine whether this more radical approach is sufficient to wipe out these very malignant carcinomas.

I recommend that all ophthalmologists who deal with this problem scrutinize Dr. Reese's complete paper in detail, for it is the most practical publication on the clinical aspects of this subject that has appeared in some time.

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THE LENS

GLAUCOMA AND CATARACT EXTRACTION

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Acta XVII Concilium Ophth., 1954, 233–239

Opinions differ as to the best method of treating glaucomatous patients with cataract. Most present-day authors believe that when the tension in the glaucomatous eyes can be normalized by the use of miotics, the cataract operation should be performed first; if, on the other hand, the tension remains high in spite of treatment with miotics, they think the first operation should be one intended to relieve glaucoma.

The effect of cataract extraction on the intraocular tension in 50 glaucomatous eyes was therefore reviewed in the hope of obtaining data that would provide an answer to this question. The patients were all operated on during the period from 1945 to 1953, so the operative techniques are comparable. In all cataract extractions, a total iridectomy was performed. In eyes with a previous Elliot trephine the section was made superiorly, on the corneal side of the bleb. Cyclodialysis was performed in the inverse manner, after Blaskovics. In none of the patients were any of the following conditions present: glaucoma occurring as a complication of Marfan's syndrome, microphthalmos, dislocation of the lens, glaucoma that was not recognized before the operation, or pathologic hypotony after removal of the lens because of retinal detachment or epithelial ingrowth. The effect of the extraction was considered good, if the maximum postoperative tension was 6 mm. Hg. Schiötz, or more below that recorded before the cataract operation; unchanged, if the tensions before and after operation did not differ by more than 5 mm. Hg Schiötz; and bad, if the postoperative tension was more than 6 mm. Hg Schiötz, above the preoperative readings.

Table 1 gives a synopsis of the total material of 50 eyes. In most cases the tension was not significantly altered. None of the eyes that had a raised tension before operation became worse. On the whole, however, the eyes that were changed became worse rather than better. Neither the clinical course of the disease nor the width of the chamber angle before operation had any important bearing on the result. It had been supposed that in congestive glaucoma, or in eyes with a narrow chamber angle, the removal of the lens might facilitate the outflow of aqueous and so bring the tension down. In fact, the results were just as good in simple glaucoma and in eyes with a wide chamber angle. Complications during or after cataract surgery also had less influence than might have been expected. Thus, of four eyes in which the final results were good, two had only insignificant hemorrhages into the anterior chamber, one suffered loss of

TABLE 1

Synopsis of Total Material

	Good	Unchanged	Bad	Total
Extraction without complications in				
Eyes with a normalized tension.....	2	13	6	21
Eyes with not normalized tension...	2	4	—	6
Extraction with complications in				
Eyes with a normalized tension.....	2	11	5	18
Eyes with not normalized tension...	2	3	—	5
Total.....	8	31	11	50

TABLE 2

Results in the Eleven Eyes with Tension Not Normalized before Cataract Extraction

Ceiling of tension before cataract extraction in mm. Hg Schiötz	Good	Unchanged	Bad
30–35	2	2	—
36–40	1	1	—
41–45	1	—	—
46–50	—	2	—
51–55	—	2	—

vitreous necessitating extraction with the loop, and in one the vitreous became adherent to the wound and to the upper part of the cornea. The last of these incidents illustrates the fact that even significant complications do not necessarily lead to a bad result as regards tension. It may be noted that the intracapsular method of extraction was not only followed by fewer complications, but was also accompanied by a higher percentage of good results than the extracapsular method so far as the tension was concerned.

When the preoperative condition of the eyes is taken into consideration, two points of special interest stand out. First, the effect of the cataract extraction on the tension was bad in three eyes in which the tension had previously been normalized by Elliot's operation. Second, a good effect was secured in eyes that had not previously been operated on for relief of glaucoma and that had not been normalized by miotics. Table 2 shows that in none of the 11 eyes that had a high tension before extraction was there any further increase in tension and that in 4 of the eyes the tension became lower. This is in contrast to the generally accepted opinions and should encourage ophthalmologists to undertake initial cataract extraction in such eyes.

In this series the intracapsular method with total iridectomy gave the best results. A tension of 45 mm. Hg Schiötz, is, however, the upper limit for a procedure of this type; if the tension is higher, an antiglaucomatous operation should be the primary procedure. The choice of procedures in eyes with a tension above 45 mm. Hg seems to lie between an iridencleisis and a cyclodialysis, because

the effect of an Elliot trephine operation is more apt to be spoiled by a subsequent cataract extraction than is that of either of these.

Comment: As stated by the author, there is no general agreement on the surgical procedure to be followed in eyes with glaucoma and cataract. This has always been a very difficult decision to make and most surgeons have followed the time honored custom that if the tension can be normalized, or near normalized with miotics, a cataract extraction is done as a primary procedure. It is assumed, of course, that the patient is known to have glaucoma and that the increased intraocular tension is not due to a swollen lens or to a toxic product from a mature cataract. The results have been analysed, and the fact that out of fifty cases, 16 per cent had an intraocular tension following surgery of six mm. Hg below that which was recorded before surgery, 62 per cent were unchanged, and 22 per cent had a higher intraocular pressure following surgery, follows, more or less, the previous published reports.

Based on eleven patients, however, the statement, "a beneficial effect was seen in eyes which had not undergone antiglaucomatous operations before and which were not normalized by miotics," would seem rather presumptuous. As a rule, antiglaucomatous surgery on aphakic eyes is not as successful as in phakic eyes. The exception to this may be those patients who have developed posterior synechia following delayed formation of the anterior chamber. Any filtering operation complicates the cataract extraction procedure, but in the reviewer's opinion, if the pressure cannot be reduced to near normal limits with miotics, it would be safer to perform a filtering operation prior to cataract extraction. The exception to this might be those patients with chronic narrow angle glaucoma in which it might be expected that a broad complete iridectomy would reduce the intraocular pressure. This, of course, could be done at the time of the lens extraction without adding any difficulty to the procedure.

P. ROBB MCDONALD

PERSONAL EXPERIENCE WITH THE EXTRACTION OF SUBLUXATED AND LUXATED LENSES

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Acta XVII Concilium Ophth., 1954, 573–578

Subluxation and luxation of the lens may be due to various causes, especially disease and trauma. Many risks are associated with the surgical treatment of such eyes. Some complications, such as loss of vitreous and gaping of the wound, are direct; others, such as infection and severe astigmatism are remote. In the last 40 years or so, however, new techniques in anesthesia and operative procedures have been introduced to lessen these risks and to make the surgeon's task easier.

Blocking of the facial nerve (akinesia) reduces the pressure and tension exerted

by the lids on the globe, and blocking of the ciliary ganglion by retrobulbar injections of local anesthetics, such as procaine, decreases the intraocular tension and makes the vitreous dormant, so to speak. In addition, retrobulbar injection near the apex of the muscular cone of the orbit causes immobility of the globe and this increases the ease with which surgical procedures can be carried out. Fixation of the superior rectus by suture, or the blocking of the superior rectus, can also be used to facilitate intraocular operations that have to be performed from above, especially in unruly patients. Pentothal sodium basal anesthesia is of great value in patients in whom nervousness prevents the use of local anesthesia. Finally, the introduction of spreading agents (hyaluronidase), which increase the extent and duration of local anesthesia, and the intravenous use of curare and its derivatives to promote relaxation have added much to the effectiveness of anesthesia.

Preplaced sutures will either prevent the loss of vitreous or keep it to a minimum. Various methods can be used in the placing of the sutures, and the operator is free to choose whichever one he thinks best in a given case.

Since most subluxated and dislocated lenses are immature, the intracapsular method of extraction seems best. The capsule forceps, however, cannot be successfully applied to the luxated or subluxated lens. The author, therefore, always resorts to looping in dealing with such cases. The operator should determine the meridian at which the incision will have to be made, taking care to have it correspond to the place where the zonula is weakest, torn, or missing. Complete pupillary dilatation beforehand helps in finding this area. It is here that the loop has to be insinuated behind the lens; otherwise, the lens will have to be tumbled during delivery.

Diathermy, applied either by Jess's needle or Lacarrere's electrode, however, has been the preferred method of dealing with luxated or subluxated lenses in recent years, even when the displacement of the lens followed an attempted intracapsular extraction by the phacoeresis or the capsule forceps method. The diathermy needle must be well insulated, except a few millimeters from its tip; if the electrode is used, the wires must be long enough to reach the nucleus of the lens when in action. The diathermy current must also be strong enough; otherwise, the coagulation mass around the needle will not be great enough to withstand the pull and will give way during the traction made on the lens, which is surrounded by liquid—the aqueous humor and the vitreous. A current of 60 milliamperes for Jesse's needle and one of from 90 to 120 milliamperes for Lacarrere's electrode should be sufficient.

The section must be large enough to allow delivery of the lens. If, after the section has been made, the lens comes forward so as to lie behind the cornea, the operator may succeed in bringing it out and engaging it into the lips of the wound by pressure on the limbus on the opposite side of the wound, and by depressing the scleral lip with an instrument in the other hand.

At times, when an eye is being prepared for phacoeresis, the lens will be found bathed in vitreous (primary or embryonic vitreous) which pours out as soon as the section is completed, or even before. On many occasions, the lens

can be extracted with the erisiphake, if it is well applied to the surface of the lens, without aspirating any of the intraocular fluids; but if it is found that the cup (erisiphake) is beginning to suck out the vitreous, the suction must be discontinued and the methods previously described must be resorted to. Once the lens is out, the suture is tied close to the wound; other sutures are then put on either side of the first one so as to bring about complete closure of the wound.

If the lens is in the anterior chamber, eserin or Fluoropryl is used before operation, and the lens may be fixed with a Bowman's needle passed from the limbus. If the lens is wandering in the vitreous chamber, Jess's method of diathermy may be preferred; if it is fixed between the ora serrata and the retina, a longitudinal or equatorial incision of the sclera and choroid must be made after some transscleral diathermy applications to prevent hemorrhage and remote detachment of the retina. The incision must be related to the locality where the lens is held.

In one of the author's cases, in which the lens was wandering between the patellar fossa and the vitreous chamber, extraction was successfully accomplished by the following method: At the beginning of the operation, the patient was made to lie face downward on the operating table, and the author lay on the floor facing him. The lens was then fixed by thrusting a sewing needle 4 cm. long through the sclera, 3 or 4 mm. behind the limbus at the horizontal meridian. The patient was then placed on his back and the lens was extracted by phacoeresis.

Surgeons faced with the problem of a luxated or subluxated lens should not decide hastily on extraction; occasionally, some other procedure will ward off a bad end or produce a better result, at least temporarily.

Comment: The extraction of a dislocated lens is always a challenge to the surgeon. There are few eyes that can tolerate a luxated lens, though there are many eyes that have tolerated a subluxated lens for many years. It takes considerable clinical judgment to decide when a subluxated lens should be removed. Undoubtedly, many eyes have been lost from injudicious attempts to remove a subluxated lens. The removal of a subluxated lens in a young individual with Marfan's syndrome almost invariably results in the loss of a small amount of formed vitreous. The use of a diathermy needle to fixate the lens and facilitate its removal would hardly seem justified. The erisiphake, if carefully applied, will be successful in a fair percentage of cases. In other cases, one may be able to grasp the upper pole of the lens with capsule forceps and deliver the lens head-on. Unless the lens is completely dislocated, there is little excuse for removing it with a loop. One can use a loop to support the lens prior to grasping it with capsule forceps, but to deliver rapidly a subluxated lens with a loop only invites more disturbance of the vitreous than necessary. The removal of a lens from the posterior chamber by a transscleral approach would appear to be a rather heroic procedure. The transfixion of a lens in the anterior chamber or in the patellar fossa by means of a needle has been suggested in numerous textbooks. The only way that this could possibly be accomplished is by the author's method in which a small short needle was thrust through the eye and the lens while the patient was on his face and then the patient was turned on his back. If one attempts to do this with a knife needle the lens invariably slips off and the eye is damaged as the patient is being turned from one position to the other. Luxated lenses in the posterior chamber, however, can frequently be irrigated toward the anterior chamber and then grasped with a loop or forceps. The

vitreous, in most instances, is fluid and is not disturbed by a well-directed stream of saline. The problem of a subluxated or luxated lens is a most difficult one, and its removal should not be attempted by the inexperienced surgeon. Though the results are sometimes spectacular, approximately 50 per cent of the patients with this condition either become blind or end up with 20/200 or less vision.

P. Robb McDonald

DIAMOX IN DELAY IN REFORMATION OF THE ANTERIOR CHAMBER AFTER OPERATION FOR CATARACT

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Bull. Soc. d'Ophtal. de France, 1955, 613–614

Secondary glaucoma following cataract removal has been said to be due to a delay in the reformation of the anterior chamber, which in turn is caused by defective coaptation of the sclerocorneal wound leading to leakage of the aqueous as quickly as it is formed. Two remedies are possible: either to close the leak, which is often undetectable even by the dye test, or to reduce the flow of the aqueous and so help the process of cicatrization. The second of these can apparently be accomplished by the use of Diamox, which reduces the production of aqueous by inhibiting carbonic anhydrase. Since July, 1954, Diamox has been used successfully by the author in seven patients in whom reformation of the anterior chamber was delayed; the results in the earliest cases were so good that he now starts the treatment as soon as he sees that the chamber is flat. A dose of 500 mg. of Diamox, given half in the morning and half at night, is generally sufficient. Needless to say, this treatment is applicable only to invisible leaks and not to large gaps in the wound.

Comment: A few case reports are appearing in the literature concerning the use of Diamox in reforming the anterior chamber following cataract surgery. A shallow, or nonexistent anterior chamber, can be a very serious complication. In most instances it is due to a leaking wound, even though this may not be demonstrable by the usual methods. There is no question that if a leaking wound can be demonstrated, it should be repaired surgically. In those cases, however, in which a leaking wound cannot be demonstrated, it may be safe to try Diamox for twenty-four or forty-eight hours. It has been postulated that Diamox causes the chamber to reform by reducing the amount of intraocular fluid that is formed and therefore reducing the pressure which permits the wound to heal more securely. To date, no one seems to have offered a better explanation. A shallow anterior chamber, however, should not be allowed to persist, and if Diamox is not effective and a choroidal detachment is present, in the reviewer's opinion, one should evacuate the subchoroidal fluid and fill the anterior chamber with air or saline. This is a relatively safe procedure and usually results in quick reformation of the anterior chamber.

P. Robb McDonald

MONOCULAR AND BINOCULAR REACTIONS OF THE LENS

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Acta XVII Concilium Ophth., 1954, 1088–1100

Reactions of the lens may be divided into (1) those occurring when the capsule is intact and (2) those occurring when the capsule is ruptured. When the capsule is intact, the lens may become cataractous, it may swell, it may change in shape, it may become luxated, or it may develop capsular exfoliation. As long as its capsule is intact the lens does not cause or participate in inflammatory reactions.

When the capsule is ruptured many reactions can follow the release of lens material into the eye. Lens cortex in the anterior or posterior chamber can react in several ways. It can remain as an *apparently inert substance*, causing no reaction whether absorption is slow or rapid. The lens cortex can act as a *simple foreign body* and attract foreign body giant cells and only a few other inflammatory cells.

The lens cortex can act as a *toxic material* producing a great inflammatory response. When the posterior capsule of a hypermature lens ruptures, the liquid cortex acts as a chemical irritant. If the cortex is solid, the inflammatory cell reaction is greater. The toxic reaction is always unilateral.

The lens can act as an *allergen producing endophthalmitis* phaco-anaphylactica. Here the inflammatory reaction is as great as, and usually greater than, that of the phacotoxic type. There is adequate evidence that bacteria or their toxins amplify the inflammatory reactions produced by the weakly-antigenic lens substance.

Not everyone accepts endophthalmitis phaco-anaphylactica as a disease entity. Many prefer to speak of "lens-induced endophthalmitis," "lens reaction," "reaction to retained lens matter," or "reaction to lens protein." Some believe it is only a toxic reaction and does not involve allergy.

The best treatment for the phacotoxic reaction, endophthalmitis phaco-anaphylactica, and the iridocyclitis with secondary glaucoma which follows leakage of fluid cortex from a hypermature lens is prompt removal of liberated lens material or intracapsular extraction of the leaking hypermature lens.

CASE REPORT

A 61-year-old white female had a left extracapsular lens extraction with a complete iridectomy. Eight weeks following surgery the eye was red, tender, hypotonic, and the inflamed iris was bound to the capsular and cortical remnants of the lens. There were fine white keratitic precipitates and an aqueous flare in both eyes. The left eye was enucleated and three months later the right eye was not inflamed.

The right eye became blind eight months after the original cataract extraction and was enucleated three and one half years after this operation.

Sections of the first operated eye showed phaco-anaphylaxis. The uveal

tract was heavily infiltrated, with a cellular reaction suggesting sympathetic ophthalmia. Sections of the second, or unoperated, eye showed no evidence of sympathetic ophthalmia. The lens capsule had ruptured spontaneously, and the inflammatory reaction was typical of phaco-anaphylaxis.

So far as can be determined, this is the first reported case in which both the "first" or operated eye and the "second" or unoperated eye, both showing phaco-anaphylaxis, have been subjected to histopathologic investigation. In previous reports the "first" or "second" eye alone have been studied. Some of these have been regarded as showing both sympathetic ophthalmia and phaco-anaphylaxis. Indeed, this undoubtedly occurs. However, this case illustrates that a bilateral inflammation clinically diagnosed as sympathetic ophthalmia sometimes proves to be due to phaco-anaphylaxis alone. The spontaneous rupture of the lens capsule of the unoperated or "second" eye is of especial interest.

Thus the most serious complication of extracapsular cataract extraction is spontaneous rupture of the lens in the fellow eye with consequent iridocyclitis and perhaps glaucoma. These eyes simulate sympathetic ophthalmia.

This study emphasizes that it is better to remove the intact lens or lens cortex from certain inflamed eyes even when both eyes are involved and sympathetic ophthalmia is suspected, than to hold back lest greater inflammation be induced by operative interference. Several eyes have been saved by this means, and not a few specimens suggest that removal of the lens or its free cortex would have made enucleation unnecessary. More data are needed on the intradermal injection of lens antigen and on the study of aqueous removed by paracentesis in patients with uveitis and glaucoma which might be due to the lens.

Comment: There is no more vexing question than the clinical differentiation of sympathetic ophthalmia and phaco-anaphylaxis. The reaction of the eye to a hypermature cataract may vary considerably. The presence of secondary glaucoma, signs of uveitis, and a hypermature cataract, should make one think of phacogenic glaucoma, disregarding the swollen or dislocated lens. A point mentioned by Verhoeff and repeated by Irvine is that these patients frequently have light perception with faulty projection. This is due to the opaque lens acting as an opal glass. There is no question that a number of such eyes are lost every year because the ophthalmologist is reluctant to operate on what he thinks is a nearly blind eye. Prompt removal of the hypermature lens in these cases usually results in a remarkable resolution of signs and symptoms.

The clinical diagnosis of phaco-anaphylatica is more difficult. Fortunately, with the advent of the corticosteroids, the reaction we now see is less marked than that in the presteroid area. However, in this editor's opinion, any patient with an unusual amount of cortical material in the anterior chamber and with evidence of uveitis and/or secondary glaucoma, should have the lens material irrigated out. This does not mean an attempt should be made to remove the posterior capsule and that one should attack the remaining lens material on an "all or none basis." The lens material may not be compatible with the aqueous, but it is less compatible with formed vitreous. Should vitreous be lost, only another factor to the production of secondary glaucoma is added to an already confused picture.

There are but few instances where clinical judgment is on trial as in the differential diagnosis of sympathetic disease and phaco-anaphylactica. This paper gives many good

pointers but it is only the surgeon who has "sweated out" a case or two who can appreciate the problem.

P. Robb McDonald

CLINICAL SELECTION FOR ACRYLIC LENS OPERATION

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The ophthalmologist has been faced with a serious challenge by the development of the Ridley acrylic lens operation. Those in charge of large clinics, to which selected cases are referred, are in a position to form their own opinions. Those who live with their patients in a community must not expose them to unjustifiable risks. One obvious gain claimed for the operation is restoration of binocular vision, but this is lost if cataract develops in the remaining eye. The insertion of a lenticulus on each side does not seem to be justified until more is known of the time or duration for which it can be retained without progressive degenerative changes. If the visual life of the eye is reduced, the operation may not be justified in even one eye. Individual opinions have to be based, in most instances, on a small number of observations. Progress is made by a continual fight against mass statistics. There is a great deal of sound sense in the remark made by de Roeth in 1953, when he said that the proof of a cataract operation is the visual result.

In a series of 212 cataract operations there were 11 patients who were considered suitable subjects for the acrylic implant procedure. These patients all had vision of 6/9 (20/30) in the better eye. Consequently, with orthodox procedures, they were not likely to use the eye that was operated on with ordinary cataract lenses. The eyes were not deep set and it seemed that there was adequate working space for the technical maneuvers involved in the placing of the lenticulus. The novelty of the operation was explained to the patients and their cooperation was sought. Three very successful immediate results were obtained in a music teacher and two transport workers. In these cases, the occupations of the patients were factors of importance. In four other patients, reasons were found for abandoning the attempt, and ordinary extractions were performed without any major disaster.

In one patient, the implant caused little reaction for four or five days, and then a severe iritis developed. The eye settled down again after a few weeks, but it later flared up once more and secondary glaucoma appeared. Indications were that the eye would be lost if nothing were done, and the lenticulus was therefore removed. The removal was accomplished by making an orthodox Graefe knife

incision along with a conjunctival flap. A complete iridectomy was performed and the freedom of the iris was established by sweeping a repositor around within the iris margin. The lenticulus was removed by grasping the rim with the forceps designed for its insertion. There was no loss of vitreous and healing was uneventful.

After the completion of a cataract section, the anterior chamber is only relatively empty. The residual aqueous is a valuable ally at all times. Frequently the quantity lying between the posterior lens capsule and the vitreous face acts as a synovial fluid and facilitates tumbling or rotation of the lens in the intracapsular operation. This concept of the residual aqueous is a useful one to have in mind when carrying out complex maneuvers, such as the removal of a lenticulus. The patient subjected to this procedure, who is now aphakic in the ordinary sense of the term, is unable to do more with the affected eye than count fingers; she has many floating opacities in the vitreous; and the iris shows decided necrosis. Fortunately, however, the vision in her other eye is normal. The fact that she is hypertensive may have made her an unsuitable subject for the operation from the beginning.

Necrosis of the iris, in the restricted sense of destruction of the cellular elements while the fibrous elements are preserved, has been noticeably present in all of the patients. Necrosis is different from atrophy. A typically necotic area in the iris appears swollen and edematous, and ghost-like because of the absence of nuclei. A typically atrophic area in the iris, on the other hand, appears thin, condensed, and very cellular. These two different conditions may occur in the same iris. In simple atrophy, the pigment layer becomes thin and condensed, corresponding to a similar transformation in the overlying stroma, but it remains *in situ*. In necrosis, the reverse is true. The uveal pigmented layer of the iris becomes disintegrated. Histologically the layer becomes thicker and fragmentary and tends to fall away. This process of necrosis can be observed very readily in patients with an acrylic lenticulus within the eye by means of a modern slit-lamp in which the axis of the microscope and the beam of light can be made coincident. By ordinary methods of visual examination, the iris may look healthy, but by transillumination or by slit-lamp examination sectors of the iris become relucent. No increase of this process, however, has been found in the patients in whom a lenticulus has been present for more than two years. Apparently, therefore, it occurs as part of the initial reaction and is responsible for the extensive pigmentary deposits which are to be seen on the posterior surface of the lenticulus. The author's patients have been examined at intervals of two months, in so far as practicable, and the degenerative process does not seem to be progressing.

Myopia is a contraindication for the implant operation and so too are diabetes and hypertension. The acrylic implant, however, has a limited place in ophthalmic surgery, and can be used especially in patients who have cataract that is more advanced in one eye than in the other. In traumatic cataract, care must be taken to see that the lens is not partially dislocated and that the zonule is undamaged. A patient with monocular radiation cataract has had a brilliantly successful

result of over two years' duration. At the other extreme is the old lady with hypertension who required removal of the lenticulus and who is not likely to attain useful vision in an eye which did not have useful vision before the operation. Between these two extremes there are patients who are well satisfied with the results of the operation. It may be that, as in the acrylic arthroplasty operation, the patients will obtain a better functional result at the cost of earlier deterioration. They are certainly subject to their own special complications, such as iris necrosis and dislocation of the implant.

The future of the procedure will depend on the time spent in the initial selection of the patients and the care with which subsequent observations are made. If the visual life of the eye is reduced, the optical advantage must be discounted.

Comment: Despite many critics, more and more surgeons are attempting the implantation of an acrylic lens in either the petellar fossa or in the anterior chamber in patients with a unilateral cataract. The author is a well known surgeon, and has attempted the Ridley operation in approximately five per cent of a series of 200 and some patients with cataract. Of the eleven patients elected to have this procedure, in four the operation was abandoned, and in one the post operative reaction was so severe that the lens had to be removed. The six successful cases apparently are quite happy with their acrilic implant. Just what the final outcome will be concerning the use of acrilic implants, is not known. It is certainly not an operation to be performed by the occasional operator. The hazards of aphakia would appear to be great enough without introducing any others until further evaluation of this procedure has been made by those who are doing it more or less routinely.

P. Robb McDonald

OCULAR MOVEMENTS

THE PSYCHOLOGIC FACTOR IN DIPLOPIA

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Acta XVII Concilium Ophth., 1954, 1771–1785

More than any other eye symptom, binocular diplopia calls for a mastery of applied physiological optics, of eye muscle disturbances, retinal physiology, applied neurology, and clinical medicine, and, what has heretofore been largely neglected, a psychologic evaluation of the patient. Without an adequate clinical study, however, one is in no position to undertake a psychologic survey (the term psychologic as used herein includes also the elements designated as psychosomatic), because, unlike other head symptoms such as headache or vertigo or dizziness which are largely subjective and often unexplained, diplopia is revealed by outward signs that have hitherto not been sufficiently explored. These signs are the positions of the corneal light reflexes in both eyes. If these reflexes are in their normal pupillary positions in line with both foveas behind, one should expect normal binocular single vision. If, on the other hand, the corneal light reflex is displaced in one eye as a result of eye deviation, two images of a light are seen unless sight in the deviating eye is momentarily or permanently suppressed. The greater the displacement of the corneal light reflex from the normal pupillary position the greater the separation of the double images. Moreover, the position of the displaced corneal light reflex in relation to its normal position indicates at a glance in what direction and to what extent the secondary image is being projected, because the displacement takes place in a direction opposite to the deviation and the light impulse proceeding backward from the corneal light reflex strikes a peripheral or extrafoveal sensitive retinal point. The secondary image reflexly projected forward through the displaced corneal light reflex indicates the spot on the extrafoveal retina which "sees" this secondary image.

A trained examiner can determine double vision without have to question the patient or even use a red glass, simply by observing the patient and noting his psychologic responses, head position, facial and lid appearances, and the positions and movements of the eyes. The head is often turned or tilted to relieve a weak or paralyzed eye from turning in a direction opposite to the tilt, and incidentally to avoid double vision. Patients with true diplopia often appear uncomfortable and their facial expression differs from that seen in hysteria or malingering. In some instances, the lids of one eye are kept closed to avoid seeing double, or both eyes may remain open and there may be a slight alternation of eye movements which obliges the person to look first on one image and then on the other.

A true binocular diplopia presents the following characteristics: (1) The patient sees two images at the same time without having to move his eyes from side to side. The secondary image emanates from the corner of the eye that deviates. (2) When either eye is covered, one of the double images disappears, proving that a binocular conflict is the basis for a binocular diplopia. (3) A prism correctly placed over either eye brings the separated images together and therefore helps to prove the correctness of the patient's complaint. With it, the corneal light reflexes are restored to their normal pupillary positions in both eyes. The confirmatory prism reflex test thus guides one in differentiating a true from a false diplopia, and true diplopia from visual suppression.

It should be noted that patients may think they are seeing double when actually sight is blurred as a result of cataract or glaucoma or a corneal scar. A colored glass should not be required to determine whether a patient is seeing double. It often awakens a secondary image in an eye that is otherwise quiet because of visual suppression. It may also yield a false reading by releasing any latent attempt at binocular fixation. When visual suppression is present the changing of the strength of a prism leads to a change in the position of the corneal light reflex without corresponding predictable image changes. The factor of anomalous retinal correspondence in spontaneous diplopia is a negligible one and can usually be discounted unless other evidence presents itself.

Often, the assumption is made that diplopia must be associated with ocular nerve paralysis, when in fact it may arise from conditions other than paralysis of the ocular nerves. These include (1) eye muscle weakness with or without accompanying ocular nerve paralysis; (2) innervational spasm or excitation rather than paralysis; (3) fusional imbalance or fusional breakdown, sometimes erroneously classified as psychologic; (4) ametropia leading either to fusional imbalance or to impaired visual acuity; and (5) a central lesion that has resulted in supranuclear rather than infranuclear paralysis, that is, paralysis of convergence or divergence.

The aim of the psychologic investigation, which should proceed concurrently with the clinical investigation of the patient, should be to trace the reason for double vision and to find out whether it is true or false; to ascertain whether it is feigned; to determine whether a false diplopia points to normal physiologic self-induced double vision, as in alternating strabismus; to study the part played by psychologic elements in alarming horror fusionis, whether of operative or nonoperative origin; and to instill hope and confidence in the patient who is alarmed because of his double vision. Above all, it should be borne in mind that unless the proper clinical and psychologic evaluation is made, the patient's eye symptoms will not be alleviated and that minor eye symptoms may even become worse if the mental factor is not appreciated and the patient reassured. On the other hand, when the psychologic basis for binocular diplopia has been found, and the patient's clinical status is clearly understood, treatment based on the psychologic evaluation often leads to the disappearance of the eye symptoms as well as to mental recovery.

THEORETIC AND PRACTICAL VIEWPOINTS CONCERNING A NEW MUSCLE SCHEME

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Ophthalmologica, 1955, *130:* 53–65

The scheme symbolizes muscle function and consequently does not position the muscles according to their anatomic position but in reference to their action. The figure makes evident: (1) the functions of each of the muscles; (2) the monocular muscle associations; (3) the binocular associations; (4) in the case of muscle weakness: (a) anomalies of the primary position (b) compensatory head position (c) anomalies of ocular movement (d) position of images in diplopia (e) oculo-vestibular reflexes.

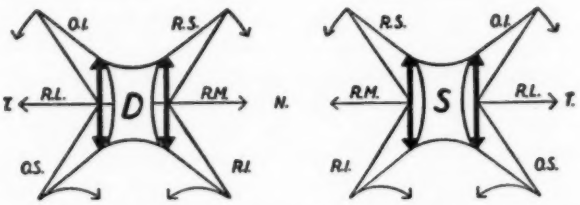

FIGURE 1. A new muscle scheme. (Reproduced by courtesy of the Authors and Ophthalmologica.)

The medial and lateral recti muscles do not require a detailed discussion in that their functions are obvious. The vertical muscles have three actions: vertical, horizontal and rotatory (intorsion or extorsion). The horizontal and vertical action is shown as a resultant by the direction of the triangle; it is evident that the inferior oblique is an abductor and levator and the superior rectus a levator and adductor. The torsion action is shown by the direction of the arrows at the apex of the triangles and indicates the direction of movement of the 12 o'clock meridian of the cornea.

The magnitude of the three functions varies with the position of the eyes. The depressor and levator effects of the oblique muscles are most marked when the eyes are turned inward in adduction while the vertical actions of the superior and inferior recti are greatest in abduction. This is made evident by the vertical arrow at the base of the triangle; its position relative to the apex of the triangle indicates the direction of greatest vertical effect. It can be seen that the right inferior oblique and the left superior rectus exert their greatest levator effects to the left. The maximum levator effect of the right inferior oblique muscle occurs with inward rotation and its strongest torsion effect occurs with the eye abducted, in which position the vertical action is practically abolished.

With the aid of the scheme the most important movements of the eyes,

the functions of the individual muscles, and also, the monocular and binocular coordination, can be demonstrated. The scheme is an aid, also, in the analysis of disturbances in position, movement and of diplopia in cases of paresis.

The primary deviation in case of paresis of the right superior rectus is shown by the direction of the median of the three triangles which remains after the triangle which represents the paralyzed muscle has been covered. The compensatory position of the head corresponds with the direction of the pyramid which symbolizes the paralyzed muscle itself. The position of the face and of the chin corresponds with the direction of the arrow which is placed at the base of the cone. Limitation of movements is greatest in the direction of the triangel which neighbors the deficient muscle. The secondary deviation is indicated in the scheme of the healthy eye by the triangle which parallels the paralyzed muscle. The advantages of the scheme "(Keilschema)" are its didactic significance and its applicability to cases, in which one depends exclusively on the examination of the movements of the eyes.

Comment: Schematic presentations of the action of the extraocular muscles and of the defects resulting from paralytic conditions of these muscles have frequently been proposed as a mnemonic aid. They must, therefore, in the first place be judged from the standpoint of their didactic value. Experience has shown that the effort of remembering the scheme is often greater than that required for remembering the few simple rules by which the action of the extraocular muscles can be described and which these schemes attempt to represent visually. In order to master the scheme the student must have assimilated the rules and the scheme becomes superfluous. Simple as the rules are, they are not easily represented graphically in a single scheme and the schemes are, therefore, often ambiguous or difficult to understand. Thus in the proposed scheme the arrows intended to indicate in what direction of gaze the vertical muscles have their main elevating and depressing action are not helpful and the fact that their torsional action is greatest in the opposite direction of gaze is not at all registered.

The strongest objection to all the schemes derives from the fact that they fit individual clinical cases only rarely. When confronted with an acute paralysis of a single extraocular muscle the scheme works out very satisfactorily, but these cases are easy to diagnose without a scheme. But when the patient has a complex clinical picture—and these are much more often encountered than the simple pictures—when multiple congenital pareses are present, when pareses are superimposed on preexisting latent or manifest deviations, when supranuclear abnormalities intervene, when the patient's habitual head position does not fit the rest of the clinical picture, then the schemes are of no help. What is of help is an understanding of the action of the individual muscles, derived from a knowledge of the relation between the muscle planes and the coordinates through the center of rotation of the eyes, a knowledge of the factors which determine the habitual head carriage, a knowledge of the physiology and pathology of the neuromuscular anomalies of the eyes. To be sure, this is a complex subject baffling not only to the beginner, but many years of experience in teaching the subject have shown that it is not made easier by schematic presentations intended to simplify it.

HERMANN M. BURIAN

OPTIC NERVE AND HIGHER CENTERS

LONG-CONTINUED INTRAVENOUS ADMINISTRATION OF HISTAMINE IN CASES OF LESIONS OF THE OPTIC NERVE, RETINA AND CHOROID: REPORT OF AN 11-YEAR STUDY

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Attention has recently been called to the improved visual results that can be obtained by continuing corticotropin therapy for intravascular lesions beyond the time usually considered adequate. Experiences in the treatment of ocular lesions with intravenously administered histamine also indicate that treatment with this substance is often discontinued too soon. It is impossible to tell from the ophthalmoscopic appearance of the optic disks or of chorioretinal lesions when the maximal expected vision has been obtained. Under prolonged treatment, useful vision has been restored to many patients with lesions that had previously been regarded as irreversible.

During the last 11 years, a rather large group of patients with optic and retrobulbar neuritis, chorioretinitis, and chorioretinal degeneration have been given histamine intravenously for long periods of time with restoration of normal or occupationally useful vision in many cases.

Histamine, which is the most potent agent known to medical science, must be regarded as a hormone. It can be isolated from practically every tissue in the human body, except that of the central nervous system and the peripheral motor nerves. The exact manner in which histamine is held in the cells of the body is not known.

The patients in this series were given a 1:250,000 solution of histamine base, by the intravenous drip method, at rates varying from 18 to 60 drops a minute depending on their age and tolerance. Treatment lasted for 1½ hours and was carried out daily, every other day, or less frequently, for periods ranging from a few months to 9 years. No untoward reactions have been observed in any of the patients, and hospitalization is not necessary.

The vasodilating effect of histamine is observed in the arterioles, venules, and capillaries. Studies made during treatment indicate that the flow of blood to the central nervous system and presumably to the eye is increased approximately 300 per cent. The maximum number of treatments administered in a period of 9 consecutive years to a given patient with retrobulbar neuritis was 913; the maximum number administered to a given patient with central chorioretinitis in a period of five consecutive years was 818.

Analysis of the results obtained in patients with lesions of the optic nerve

shows that good reading vision was secured in 61 per cent of all the eyes treated and in 12 of 17 eyes (71 per cent) with acute retrobulbar neuritis. This percentage would have been higher if all the cases in which the vision returned to normal before the patient had received 60 intravenous injections of histamine had been included in the calculations.

Histamine is particularly effective in the treatment of primarily edematous lesions such as central angiospastic retinopathy. Although in most cases of this type the tendency is toward rather rapid spontaneous regression of the edema, it becomes chronic in some cases unless appropriate treatment is instituted. In cases of hemorrhagic and exudative chorioretinitis with macular involvement, treatment with histamine usually does not result in improved vision until the lesion is ophthalmoscopically quiescent; consequently, it should not be withheld simply because the lesion appears to be scarred when the patient is first seen. It is impossible to remove the central scotomas completely, but good or useful reading vision can often be obtained through the resorption of residual edema and perhaps by stimulating function in dormant perifoveal visual cells. In 11 of 16 eyes (69 per cent), maintained improvement in vision was secured by the histamine treatment, and good or useful reading vision was restored in eight (50 per cent).

The results of histamine administration in several different types of chorioretinal degeneration were less favorable. Definite maintained improvement was noted in only 4 of the 22 eyes treated. Good reading vision was not restored to any eyes, but was maintained in six through the presence of a small preserved isle of central vision. In some instances, treatment seemed to halt or retard progressive loss of vision. Because of the known irregular course of these degenerations, however, definite conclusions are not warranted at present.

The exact manner in which histamine acts in "healed" lesions of the optic nerve, choroid, and retina is not clearly understood. Improvement in vision cannot be explained solely on the basis of the vasodilating effects of the drug; perhaps it can best be explained by the action of histamine on the cortex of the suprarenal gland. It may be that histamine, acting on the cortex of the gland, releases hormones, some of which have not yet been identified, and that the action of these hormones on the optic nerve, choroid, and retina brings about the restoration of useful vision in patients with lesions heretofore considered beyond the reach of treatment.

Comment: The perplexing problem of how histamine may act to alter ocular pathology other than by vasodilation is perhaps answered by the authors. They suspect that histamine may release hormones from the adrenal cortex which act upon the diseased tissue. It would be interesting to know whether eosinopenia or a change in 17-keto-steroid excretion result during the treatment. In the cases of optic neuritis treated, good reading vision was obtained in 61 per cent of all eyes treated. The same percentage of recovery was reported by the American Academy of Ophthalmology and Otolaryngology symposium on diseases of the optic nerve, in 1955, in cases treated with vitamins, vasodilators etc. This was compared at that time with figures which showed about the same level of recovery with the use of steroid therapy. Statistically, then, the results of all methods are about the same.

The method recommended by the authors involves repeated intravenous infusions over long periods, and would not be economically feasible for many patients seen by the ophthalmologist.

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ARTERIOSCLEROTIC OPTIC ATROPHY (PSEUDOGLAUCOMA)

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Eye Digest (Watson Gailey Eye Foundation), 1956, *1:* 29–33

On ophthalmoscopic examination, patients with arteriosclerotic optic atrophy are found to have optic atrophy of the so-called primary type with pallor and cupping resulting from axon degeneration without gliosis or fibrosis in the cup. The cup margin often shows depression and degeneration produced by sclerosis of cilioretinal vessels (better designated as ciliopapillary vessels). The resulting appearance of an atrophic shelf surrounding the deep cupping is important in diagnosis because it indicates sclerosis not only of the cilioretinal vessels but also of those farther upstream—the ophthalmic and internal carotid arteries and their branches which supply the optic nerves and chiasm. This sclerotic rim or shelf must be differentiated from the scleral crescent of developmental origin which has no clinical significance.

As a rule, patients with arteriosclerotic optic atrophy are past middle life and show evidences of arteriosclerosis elsewhere in the body. The visual field loss which is their chief complaint results either from destructive pressure upon the optic nerves and chiasm, or from the inability of the arteriosclerotic vessels to supply them with adequate nourishment.

Destructive pressure on the axons may occur either in the chiasmal area, from the large vessels which normally are in contact with the chiasm and the optic nerves, or within the narrow confines of the optic foramen where the ophthalmic artery is in contact with the optic nerve. An almost constant observation at postmortem is the grooving of the chiasm by the knee of the internal carotid arteries. Grooving of the optic nerve by the ophthalmic artery in the optic foramen is not observed; however, the space in which the nerve and the artery are in contact is constricted and does not permit expansion.

Arteriosclerotic optic atrophy may require differentiation from the primary optic atrophy produced by various other conditions causing pressure in these locations, notably, in the chiasmal area, adenoma of the hypophysis, craniopharyngioma, meningioma of the tuberculum sellae, internal hydrocephalus with dilatation of the optic recess, and aneurysms in adjacent vessels; and, in the

optic foramen, constriction of the bony foramen as in Paget's disease and dilation of the bony foramen with compression of its contents by tumors such as meningiomas.

In addition to the history, roentgenologic examination is of great importance; in particular, skull films should be made of the sellar area to show calcium deposits and bone changes. Similarly, films should be made of the optic foramen to show bony constriction or dilatation. Arteriograms and air studies may also provide valuable diagnostic information.

The most typical visual field losses are nasal or altitudinal and are caused by involvement in the chiasmal area. They can be differentiated from the usual bitemporal loss produced by pituitary adenoma and possibly other tumors and internal hydrocephalus. Involvement of the optic nerves leads to peripheral segmental loss and more rarely to concentric constriction or central scotoma; these losses, however, are not characteristic and are not necessarily of diagnostic value. Post mortem studies show sclerosis of the larger vessels and proliferative endarteritis of the smaller ones; the chiasm and optic nerves are apparently first affected in the vicinity of the involved blood vessels with subsequent extension of the degeneration in both directions in a kind of cavernous atrophy.

Differentiation between arteriosclerotic optic atrophy and temporal arteritis, which also occurs in old persons with arteriosclerosis, may be based on the fact that arteritis is characterized by cellular infiltration with various stages of inflammation frequently terminating in granulation and necrosis, while in arteriosclerosis alone the degenerative process is less acute and the progress less rapid, without pain or fever and with less marked systemic signs of generalized vascular involvement. The intraocular tension in arteriosclerotic optic atrophy, unlike that in glaucoma, is normal, and the characteristics of the condition are so clearly defined as to make it a distinct entity. The use of such terms as pseudoglaucoma, soft, and low tension glaucoma should, therefore, be abandoned in favor of the more exact one of arteriosclerotic optic atrophy.

Comment: The author's point is well-taken as to the use of the term "arteriosclerotic optic atrophy" rather than the name pseudoglaucoma. However, I still prefer to cling to the latter name as a constant reminder that glaucoma must be thoroughly ruled out in such cases. The appearance of the optic discs and the visual field defects which are very similar to those of glaucoma make tension studies, outflow tonography, and repeated examinations mandatory—especially in the age-group involved. Certainly, any case with such atrophy should also be studied thoroughly for chiasmal tumor, as Dr. Lyle has pointed out. The statement that arteriograms are of importance in reaching a final diagnosis is one which might have to be "sold" to the neurosurgeon responsible for the arteriography. He would be understandably reluctant to perform such a diagnostic procedure in an elderly arteriosclerotic patient, since a hemiplegia might well result. In fact, one of my neurosurgical colleagues, faced with an elderly patient with chiasmal field changes and optic atrophy, felt that direct surgical attack on the chiasm was safer from the circulatory point of view than arteriography.

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SPASM OF FIXATION

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Am. J. Ophth., 1955, *40:* 724–730

Fixation refers to a maintenance of the posture of the eyes by tonic contraction of the ocular muscles so that the retinal images of the object which is fixed fall upon the two foveas. It may be considered as consisting of two components—a voluntary cortical mechanism for coarse adjustment and an involuntary reflex subcortical mechanism for finer and more delicate adjustments. The voluntary mechanism utilizes the pathways for conjugate lateral and vertical gaze. Movements for lateral gaze are probably initiated in the oculogyric center in the Betz cells of Brodman's area 8, located in the posterior portion of the second prefrontal convolution. The fibers which arise in these cells pass through the corona radiata and enter the internal capsule. These fibers cross over to the opposite side in the midbrain and upper part of the pons. From here, the assumption is that they enter the center for conjugate gaze probably situated in front of the sixth nerve nucleus near the midline. From this center some fibers are probably distributed to the ipsilateral sixth nerve nucleus, while others cross the midline and ascend in the posterior longitudinal bundle to reach the third nerve nucleus of the opposite side.

As yet no cells have been identified in the frontal cortex as subserving the function of vertical conjugate movements. However, if the horizontal extraocular muscles are severed, vertical movements have been obtained by stimulation of the oculogyric center in the posterior portion of the second prefrontal convolution. Fibers for vertical gaze have not been identified in the internal capsule, but they have been identified in the region of the superior colliculus and are thought by some to pass thence to a hypothetical elevator and depressor center just below the superior colliculus. From these hypothetical centers, they are believed to enter the posterior longitudinal bundle to be distributed to the appropriate oculomotor nuclei.

Little is known with certainty about the centers and pathways of the involuntary fixation reflex. The afferent pathway, however, is unquestionably composed of the visual fibers from the retina to the calcarine cortex. There is no agreement as to the layer of cells of the visual cortex in which the motor fibers begin. Whatever their starting point, however, they pass downward from the optomotor area in or around the calcarine fissure to the medial side of the visual radiation and through the posterior portion of the internal capsule to the basal ganglia and the lower conjugate centers.

The voluntary mechanism probably exerts an inhibitory influence upon the subcortical (reflex) mechanism. It seems that if the voluntary fixation mechanism is abolished or destroyed, an exaggeration and intensification of the reflex

fixation mechanism may supervene with a resultant spasm of fixation. This fixation spasm is initiated and perpetuated by proprioceptive impulses from the ocular muscles themselves, resulting initially from the fact that retinal impulses are continually acting upon an uncontrolled cortical mechanism.

Spasm and intensification of the fixation reflex is usually associated with a paresis or paralysis of voluntary conjugate lateral or vertical movements and voluntary convergence, with a retention and intensification of the proprioceptive reflexes. Paresis or paralysis of voluntary conjugate lateral or vertical movements is shown in a typical case when the patient is unable to look to either side on command or to an object which he can see placed on either side of him. On attempting to carry out such a command, he will usually turn his head in the direction in which he has been asked to look. Paralysis of convergence may also be present, but more often, although sudden convergence on a near object is not possible, normal convergence may occur if a distant object on which the gaze has been fixed is slowly brought forward. As a result of the intensification of the fixation mechanism, the patient must first interrupt the fixation reflex before he can move his eyes to follow an object that has been fixed. This he does by blinking, turning and jerking his head, or placing his hand between his eyes and the object of his fixation. Retention of the proprioceptive reflexes is shown by the fact that full lateral or vertical excursion of the eyes may be obtained by passively rotating the head. For example, if the patient cannot turn his eyes to the left, rotation of the head to the right causes passive deviation of the eyes to the left, for although his head is moved passively the eyes remain directed toward the point upon which they were originally fixed.

An interesting example of fixation spasm was presented by a 6-year-old boy first seen at Children's Memorial Hospital at the age of 5 years because he did not appear to move his eyes when looking at things on either side of him. His mother stated that she had noticed, when he was 16 months old, that he had to turn his head to see things instead of moving his eyes. He had been delivered at full term, after a short, abrupt labor. He was born with an occipital meningocele which was removed at the age of one month. Skull roentgen ray films showed a defect in the occipital bone in the midline. The child's development was apparently normal; however, the Stanford-Binet I.Q. rating was 73 and neurologic examination disclosed some hypotonia of all the extremities and some difficulty in speech.

Examination of the extraocular muscles revealed a preference for fixation with the right eye. Upward and downward gaze appeared normal. The patient was unable, however, to look to either the left or the right on command. Instead of moving his eyes, he instinctively turned his head or his head and shoulders to the side toward which he was attempting to look. Full lateral excursion of the eyes on passive movement of the head and interruption of the fixation reflex by blinking in order to move the eyes were also present. Convergence was impossible. The patient was observed for one year, and during this time some improvement seemed to take place.

Two points deserve consideration. First, the patient had a meningocele in the

occipital region, which may have been associated with a defect in the occipital cortex, or in the internal sagittal stratum. Such a lesion, however, while it would interfere with the involuntary fixation mechanism, could in no way account for the paresis of conjugate gaze. Second, labor was short and precipitous, suggesting the possibility of birth trauma. Hemorrhage into the frontal cortex from the superior saggital venous sinus resulting in injury to the frontal oculogyric centers could easily account for the paresis of conjugate gaze. As a result of destruction of the voluntary frontal cortical centers for fixation, the involuntary subcortical mechanism would be uninhibited by the frontal cortical centers and an uncontrolled involuntary fixation mechanism would lead to spasm of fixation. In all probability, therefore, the spasm of fixation presented by this child was due to an injury to the frontal oculogyric centers of the kind described.

Comment: The patient described by the author is a fascinating problem in applied neuro-anatomy. The "spasm of fixation" with regard to voluntary movement involved *only* the horizontal movements. There is reason to believe that vertical movement is also mediated from the frontal oculogyric centers, the pattern having been established by direct stimulation in the monkey, at least. However, the author states that upward and downward gaze appeared normal. It is difficult to understand how damage to the frontal oculogyric centers as severe as hypothecated would fail to involve vertical voluntary movement as well. It would be interesting to know whether optokinetic responses were also involved in order to assess the integrity of the occipital oculogyric centers, as well as whether there was also a difference in response between horizontal and vertical movement with such stimulation. Since conjugate movement occurred on passive head turning, the vestibular inflow into the final motor pathways, as well as the median longitudinal fasciculus system and motor nuclei, appeared intact; this tends to eliminate the possibility of a bilateral pontine lesion with bilateral horizontal conjugate paralysis. Since it is known that the fibers from the cortex which mediate vertical movement enter the final motor system at midbrain levels, while those for horizontal movement enter it at pontine levels, one might place the involvement in the brain stem below the level of the midbrain.

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ACUTE CILIARY GANGLIONITIS

H. RIEGER

Linz

Deutsch. Ophth. Gesellsch., 1953, *58:* 141–146

In 1951 Rieger (Verhandl. d. Ophth. Ges. in Wien) reported two cases of an unusual syndrome characterized by the sudden occurrence of a unilateral internal ophthalmoplegia associated with retrobulbar neuritis, for which he coined the term "acute ciliary ganglionitis." In the present paper, the author

describes three additional cases of this syndrome involving a 12-year-old boy and two 40-year-old women.

In the boy, cyclitis and retrobulbar neuritis developed suddenly in the right eye during convalescence from chickenpox. These inflammations were associated with an internal ophthalmoplegia with a maximally dilated and fixed pupil and with a decrease of accommodation of 5 diopters. Central vision improved and the cyclitis subsided but the disturbance of the pupil and the accumulative paresis remained unchanged.

A right optic neuritis developed suddenly in one of the two women who had chronic tonsillitis and three devitalized teeth; disturbances of the pupil and an accommodation paresis of 3 diopters were observed simultaneously. Three months after tonsillectomy and dental repair the pupillary changes were considerably improved, the optic neuritis had subsided and normal accommodation had returned.

The third patient had 6 dead teeth, some of which were associated with dental granuloma, and she also had mild tonsillitis. A sudden pupillotonia developed which was more pronounced in the right eye and six months after the onset of this disturbance, an accommodation paresis of 1 diopter was observed in the right eye.

From the literature the author collected an additional case of a complete syndrome of acute ciliary ganglionitis and seven cases of internal ophthalmoplegia, in some of which a pupillotonia resulted. Disturbances of tendon reflexes were also present in five of the 13 patients.

The author states that some of the cases, which in practice had been considered as cases of "pupillotonia," showed at the onset acute ciliary ganglionitis or internal ophthalmoplegia, and, contrary to that seen in the typical case of pupillotonia, were characterized by the occurrence of paralysis or paresis of accommodation. In some of these cases late disturbances of tendon reflexes occurred. Consequently, the problem of differentiation of ganglionitis ciliaris acuta from Adie's syndrome, or that of including those cases within the frame of Adie's symptom complex by considering them an exceptional type of this symptom complex, requires further clarification. The absence of uniformity in the cases of pupillotonia and in those of Adie's syndrome arises from the fact that one seems to be of peripheral and the other to have additionally a central origin.

Those cases which are caused by focal infections seem likely to have considerable improvement provided that there is early and energetic treatment. The optic neuritis as well as the motor power of the pupil and particularly the accommodation may be improved. Since residual symptoms of accommodation paresis may be observed in older cases, the incidence of acute ciliary ganglionitis may be higher than presented. In the patients reported in the literature, women predominated in a ratio of 9 to 4.

Comment: The term "acute ciliary ganglionitis" coined by the author is less descriptive than "opticociliary neuritis" used by Mancall, who reported a similar case in the Archives of Ophthalmology (1955, *54:* 436). Mancall also used 2.5 per cent mecholyl to demonstrate

a pupillary constriction in the involved eye, a point in diagnosis which Rieger fails to mention. This response gives definite evidence of denervation of the sphincter. Although the same response occurs with the tonic pupil of Adie's syndrome, it is unusual to have the profound disturbance of accommodation described by both authors. It would be interesting to know whether the power of accommodation also increases in these patients with the instillation of mecholyl.

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VISUAL FIELD STUDIES FOLLOWING OCCLUSION OF THE ANTERIOR CHOROIDAL ARTERY

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Am. J. Ophth., 1955, *40:* 796–801

The visual fields of 12 persons before and after surgical occlusion of the anterior choroidal artery for the alleviation of parkinsonism were studied in an attempt to determine the effect of this operation on the visual pathways in human beings. The fact that various structures in the optic pathways may receive blood supply from the anterior choroidal artery has been demonstrated, but opinions differ in regard to the details of the problem. It has been shown that although considerable variation may exist in the territory of distribution of the anterior choroidal artery, the variations occur mostly in the so-called superficial circulation of the vessel, rather than in the deep supply to the globus pallidus. Furthermore, rich anastomoses with branches of other arteries were observed in the superficial circulation, the principal ones being in the lateral geniculate body between the anterior choroidal artery and the posterior cerebral artery.

The results of these investigations have not entirely explained the presence in some cases, or the absence in other cases, of hemianopic defects following spontaneous occlusion of the anterior choroidal artery. From a survey of the literature concerned with the syndrome of the anterior choroidal artery, it might be inferred that some of the symptoms, such as the hemianopic defect, were not actually due to the occlusion of the anterior choroidal artery *per se*, but rather to generalized cerebral arterial disease and defective collateral circulation.

As far as could be determined by clinical investigation, there was no evidence of cerebral or generalized arteriosclerosis in the 12 subjects studied in this investigation, and their blood-pressure values were within normal limits. The relative absence of visual-field defects following known occlusion of the anterior choroidal artery appears to be worthy of note. A definite visual defect persisting

into the sixth postoperative month was found in only one instance. Neither hemiplegia nor hemisensory disturbances were observed in the cases studied. In most instances, a marked and unequivocal change was produced in the tremor and rigidity, testifying to satisfactory occlusion of the deep pallidal branches of the vessel. Postoperative arteriograms were made and compared with the preoperative films in several cases in order to add further objective evidence of artery occlusion.

Previous anatomic investigations have shown that the only nervous structure which is entirely dependent on the anterior choroidal artery is the medial portion of the globus pallidus, and that the branches which supply it are the most constant of all the branches of the anterior choroidal artery. Other structures, such as the posterior limb of the capsule, the lateral nucleus of the thalamus, the substantia nigra, and particularly the lateral geniculate body, receive only part of their blood supply from the anterior choroidal artery and under ordinary circumstances can be adequately supplied by other vessels. This is apparently the reason why relief of tremor and rigidity may at times result from anterior choroidal artery occlusion without other neurologic signs. The occasional absence of hemianopsia, even in cases in which hemiplegia and hemianesthesia have been reported in patients with spontaneous thrombosis of the anterior choroidal artery, may be explained by the lesser vulnerability of the optic pathways resulting from more adequate collateral circulation.

The incidence of visual-field defects in cases of surgical occlusion of the anterior choroidal artery is low. When they do occur, the reason is likely to be found in defective collateral circulation from the posterior cerebral artery or in anomalies of distribution of the anterior choroidal artery. Overlapping blood supply from different arterial sources in all segments of the visual pathways probably accounts for the low incidence of hemianopsia in this series.

Comment: The interesting absence of hemianopsia in all but one of the authors' 12 cases after occlusion of the anterior choroidal artery has further application. In reviewing perimetric records it is soon apparent that hemianopsia on a vascular basis due to involvement of the optic tract is a rarity. The authors point out that although the anterior choroidal artery also supplies the optic tract, the only nervous structure entirely dependent upon this artery is the medial part of the globus pallidus—fortunately for their surgical approach. According to Lyle the optic tract is also supplied by the middle cerebral and posterior communicating arteries. Such a rich collateral circulation makes the optic tract almost invulnerable to vascular occlusive lesions.

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THE PUPIL

CONSTRICTOR AND DILATOR INNERVATION OF THE FUNDUS IN RABBITS

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Tübingen

Acta Neurovegetativa, 1954, *10:* 209–213

METHOD

Working on dark-pigmented rabbits with light ether-evipan narcosis, the author tested vascular responses by the intravenous injection of dyes. The findings are based on color photographs of the fundus. The intensity of staining was compared to Ostwald's color scale and the values so obtained were plotted as the ordinate, against time as the abscissa. In this way graphs of "vasoconstriction" and "vasodilatation" were obtained.

RESULTS

(A) Section of the cervical sympathetic caused deeper staining, e.g. "vasodilation," of the same degree as is found after intravenous administration of a sympathicolytic agent such as dehydroergotamine. (B) Since the parasympathetic pupilloconstrictor fibers arise from the ciliary ganglion, the author assumes that retinal vasodilator fibers arise from this ganglion also. After removal of the ciliary ganglion, the homolateral pupil dilated and the retinal vessels "constricted" for a short time. The opposite pupil likewise dilated slightly. Both pupils contracted about 1.5–2 mm. upon intravenous injection of 0.3 mg./kg. of hydergin. (C) In normal animals the fundus stains after intravenous ergotamine (see 1) the parasympathectomized eye failed to show this reaction. The animal's normal opposite eye showed a delayed staining reaction at this time. (D) After additional extirpation of the sphenopalatine ganglion on the same side, the "vasoconstriction" became enhanced on the operated side and the vessels of the normal eye also "contracted." Intravenous ergotamine now failed to elicit the staining reaction on both sides and neither pupil showed contraction after the ergotamine injection.

CONCLUSIONS

The author concludes (1) that the "vasodilation" after sympathectomy and after the intravenous administration of sympathicolytic drugs is not directly due to the lack of sympathetic impulses but to a relative increase of vasodilator influences. This is thought to be the reason why sympathetic blocking fails to affect the retinal vessels after removal of the ciliary ganglion. (2) The temporary (for several hours) vasoconstriction seen after removal of the ciliary and spheno-

palatine ganglia proves that the eye normally receives vasodilator impulses from these ganglia.

THE "PARADOXICAL" REACTION OF THE PUPIL AND RETINA

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Zentralbl. ges. Ophth., 1955, *65:* 321

In diseases of the retinal vascular system, drugs often cause reactions which differ from the expected result. The author examined the "paradoxical phenomenon" of pupil and retinal vessels in rabbits.

Twenty hours after removal of the superior cervical ganglion, a high cervical cord transection, surgical "exclusion of the interbrain", or narcosis caused miosis and vascular dilatation on the normal side and simultaneous mydriasis and vascular constriction on the previously sympathectomized side, the author assumes a system of intra-central connections, as follows: (1) After cervical sympathectomy, the "tonus" of the cilio-spinal center of Budge is depressed. (2) The parasympathetic tonus of the sphincter nucleus sinks simultaneously ("reflexly"). (3) The previously existing "independence" of Budge's center is lost and hypothalamic influences raise its depressed (due to the sympathectomy) tone. (4) A subsequent interruption of this hypothalamo-cervical connection, by narcosis or cervical transection, causes the paradoxical phenomena in the eye, because the (reflexly) lowered tonus of the sphincter nucleus "can be carried only from the hypothalamus via Budge's center."

DISCUSSION

H. J. Küchle (Munich) says he saw similar paradoxical phenomena in respect to intraocular pressure: rabbits usually show a lowering of intraocular pressure after electro-shock. After paralysing the interbrain by urethane-narcosis or by barbiturates, electro-shock is followed by a considerable rise in intraocular pressure.

Comment: While the assumption of an inverse parallelism between pupillary and retinal vascular reactions would, if proven, be of great importance and simplify many clinical problems, a great number of objections have to be raised. They are concerned both with the author's observations and, even more so, his assumptions and conclusions. The principal objections are:

(1) The author rejects the otherwise generally accepted opinion that paradoxical pupillary dilation is due to hypersensitivity of the denervated dilator muscle on the grounds that he could obtain the same results after surgical removal of both adrenals. He ignores the extensive physiological work, done by many of our best physiologists (cf. the

review by W. C. Cannon and Rosenblueth, 1949) which proves that the adrenals are not the only source of sympatheticomimetic substances. Adrenaline-like substances are poured out by the liver, the accessory chromaffine tissue, and the sympathetic nerve endings all over the body. Paradoxical pupillary dilation, just as retraction of the denervated nictitating membrane, acceleration of the denervated heart, inhibition of the stomach and intestines are only a few examples of effects obtained by such humoral influences. A general law was first mentioned by Claude Bernard as far back as 1880 and formulated by Cannon (1939) as follows: "When in a series of efferent neurones a unit is destroyed, an increased irritability to chemical agents develops in the isolated structure or structures, the effects being maximal in the part directly denervated." Paradoxical reactions have been obtained in denervated structures by stimulating the remaining sympathetic chain on the opposite side, visceral sympathetic nerves, the sympathetic fibers to the piloerectors of the cat's tail, to give only a few examples. The reactions take place in the presence or absence of the adrenals.

(2) In order to explain the phenomenon of paradoxical pupillary dilatation the author assumes a complex series of reactions (cf. Zentralbl, ges. Ophth., 1955) including hypothetical loss of "tone" of Budge's center followed by restoration of the "tone" by means of hypothalamic discharges and reciprocal weakening of the third nerve nucleus. This imaginary mechanism, called "compensation," is supposed to cause the pupillary dilatation.

The author freely assumes nervous connections without attempting to actually prove their existence. For example: (a) after section of the postganglionic fibers of the superior cervical ganglion, paradoxical pupillary dilation appears. But no ascending fibers are known by which the superior cervical ganglion could influence Budge's center. (b) According to our present knowledge, the sympathetic motor path from the hypothalamus via the cervical cord and sympathetic chain to the iris is a purely efferent system; there are no known afferent connections by which a "compensatory" discharge of the hypothalamus could be brought into play. (c) Neither an afferent path from Budge's center to the third nerve nucleus nor (d) a vasomotor path from Westphal-Edinger's nucleus to the retina via the ciliary and sphenopalatine ganglia have been demonstrated. It would be equally unacceptable if the author assumed that nervous impulses pass over the efferent connections in the wrong, i.e., afferent direction. It should finally be mentioned that the activity of a nerve center may be depressed, inhibited or facilitated, but a "tonus" of nerve centers is a mystical conception.

(3) The paradoxical pupillary dilation would be a parasympathetically conditioned phenomenon if the author's assumption of "reflex lowering of the tone of the third nerve nucleus" were correct. But this concept does not agree with the fact that paradoxical dilation of the sympathectomized pupil can be elicited with equal facility after additional transection of the third nerve, removal of the ciliary ganglion, ligation of the short ciliary nerves or instillation of atropine (Lewandowsky, Klin. Mbl. f. Augenh., 1900, *38:* 129; Langley, J. Physiol., 1901, *27:* 237). Hypersensitivity of the denervated structures to circulating adrenaline has been observed decades ago and produced time and again since then. It can easily be demonstrated by intravenous injection of minute quantities of adrenaline or by local application of adrenaline on the eyes of dead animals and even *in vitro* in the excised iris.

(4) As to the vascular responses, the facts are likely to be vastly more complex than the simple coordination of pupillary and vascular events proposed by the author. In our experiments on the central control of reactions in the vascular bed of the ear auricle with simultaneous recording of arterial blood pressure, intra-ocular pressure and pupillary

movements, it has been our experience that these various factors often, but by no means always, respond together. In addition, different experimental conditions, such as variations in the level of anaesthesia, temperature, the general condition of the animal, afferent stimuli, pre-stimulation levels of the animal's blood pressure and intraocular pressure, and other uncontrolled factors profoundly affect the reactions to otherwise identical stimuli; they may even reverse them. These facts do not appear to have been adequately considered in the author's work. In our own experiments on cats and monkeys we never found contralateral reactions upon unilateral removal of the superior cervical ganglion or ciliary ganglion. Their occurrence raises the suspicion that operative trauma affected the results via central mechanisms.

[¶(5) In general, rabbits have proven to be unsuitable subjects for this type of experiment. Their autonomic regulation in contrast to that of other mammals like cats, dogs, or monkeys, contains too many unknown factors, among them (a) the strong miosis produced by stimulation of the 5th nerve or its intracerebral sensory roots, (b) frequent occurrence of a generalized vascular collapse, for instance after a simple intravenous injection or even after mere pricking of an ear vessel, (c) the slowness and long duration of many autonomic reactions or (d) the inability to compensate for changes in body position.

OTTO LOWENSTEIN

SIMPLE PUPILLOMETER

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Brit. J. Ophth., 1955, *38:* 762–763

This simple instrument for measuring pupil diameter, originally invented by Helmholtz, was used by Wenger (Comp. Psychol. Monogs., *19*, No. 4, Serial 101) in an attempt to assess autonomic balance in candidates for the U.S.A.A.F. It has been recently used fairly extensively by the writer to measure the action of drugs upon the pupil, and has been found to give accurate results.

The instrument consists of an oblong dull black card about 7 x 3″, with pinholes punched in it. At one end the two holes are 8 mm. apart vertically, and the vertical space between each pair is gradually decreased in 0.5 mm. steps, until the last two are only 2 mm. apart. The pairs are 1 cm. apart from each other horizontally.

The subject stands with his back to a wall (to prevent excess lighting of the back of the card) and looks through the holes at a distant object which is well lit (the exact amount of illumination is relatively unimportant, probably because of the very small area of the pinholes as compared with the pupil itself). The card is held close to one eye to prevent any attempt at accommodation, and the other eye is closed. The subject tries to look through two holes at once and moves the card to and fro till he finds the pair which give the correct appearance.

The subject is asked to choose the appropriate pair of holes and their distance apart is noted. The card is then taken away and handed back the other way round, and he chooses again. This performance is repeated five or more times to give material for statistical analysis. It will be found that if the patient is of average intelligence his answers will seldom vary by more than ±0.5 mm., once he has learned the method.

It is suggested that this simple instrument is of considerable value for research work upon the physiology and pharmacology of the autonomic nervous system. It might also be of some slight value in neurology and ophthalmology, and perhaps also in the study of morphinism.

Comment: Entoptic methods for pupillary measurement have been widely used since the middle of the last century. They have in the past furnished useful information in the hands of seasoned experimenters who employed them to observe their own pupillary play. As a clinical tool and "for research work upon the physiology and pharmacology of the autonomic nervous system," the method used by the author has no value for the following reasons:

(1) The method is not objective. In the time of high speed flash and infra-red photography no method should be advised which relies for accuracy on the cooperation and the intelligence of the patient. The investigators of the 19th century had no choice in this matter, but we have.

(2) Only one pupil can be measured at a time, and since the pupillary diameter normally fluctuates from moment to moment, it becomes very difficult to compare the right and left pupils. The first signs of pathology often appear unilaterally or asymmetrically. Therefore, simultaneous recording of the two pupils is necessary to a sensitive diagnostic tool. This advantage is lost in the method described.

(3) The method gives information only on pupillary size, which by itself allows no conclusion as to the state of the nervous supply of the iris. For example, miosis may be due to sympathetic weakness or to parasympathetic spasm, mydriasis to sympathetic irritation or to parasympathetic paralysis. In order to find the mechanism responsible for a given pupillary size and to gain information on the dynamic sympathetic-parasympathetic equilibrium in each patient, it is necessary to examine the pupillary reflexes.

OTTO LOWENSTEIN

SYSTEMIC DISEASE

SURGICAL TREATMENT (SURFACE DIATHERMOCOAGULATION) OF EALES' DISEASE

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Acta XVII Concilium Ophth., 1954, 215–223

Eales' disease, a clinical entity characterized by hemorrhages which invade the vitreous body in successive onsets, attacks particularly adolescents and young adults, more frequently males. The fact that the recurrent hemorrhages in young persons corresponded to lesions in the retinal veins was first pointed out by Eales himself; years later, Axenfeld and Stock showed that in many cases there is a relationship between the hemorrhages and retinal tuberculous periphlebitis, although in others no evidence of tuberculosis can be found. On the whole, it may be said that while infectious, endocrine, and toxic factors all enter into the process, the condition is basically a constitutional angiopathy comparable to angiomatosis.

Many difficulties are admittedly associated with the treatment of Eales' disease and the results achieved in the past have often been unsatisfactory. The principal object of treatment should be to prevent new retinal and vitreous hemorrhages, which, in time, cause the formation of tracts of retinitis proliferans. In the region of the periphlebitic lesions fine newly formed vessels appear and as these vessels are very fragile, they can easily become the source of new vitreous hemorrhages.

Since 1947, therefore, the authors have applied transscleral surface diathermocoagulation directly to the recent periphlebitic foci and the newly formed vessels. This method has now been used, either therapeutically or prophylactically, in 11 patients (13 eyes), 7 of whom have had no further vitreous hemorrhage (follow-up, 1½ to 6 years). In 9 of the patients, the operation was performed on the second eye; the first eye had either been lost as a result of recurrent hemorrhage, or its fundus could not be explored because of the state of the vitreous. This demonstrates the importance of systematic examination of the second eye in cases of recurrent hemorrhage of the vitreous; even when subjective symptoms are absent, examination of an apparently healthy second eye may reveal new foci of periphlebitis. From this point of view, Eales' disease poses the same problem as retinal detachment, which also requires systematic examination of the second eye for foci of degeneration susceptible to prophylactic surgical intervention.

Prophylactic diathermic treatment of Eales' disease should be considered especially for new periphlebitic foci, particularly if they are situated in the

periphery. The operative technique is the same as that for retinal detachment; however, diathermal coagulation must be strictly superficial and very slight. The coagulated zone is easily visible with the ophthalmoscope in the form of whitish chorioretinal exudation. Frequently, at the edge of the coagulation and near the vessels, hemorrhages appear in patches, but they have no tendency to invade the vitreous and are later absorbed. The prophylactic operation was performed on 5 eyes. In 3 cases the lapse of time since the operation has been 4 years and none of these patients has had a hemorrhage of the vitreous body. In one case, the results, which at first were excellent, were later impaired by a plastic iridocyclitis that appeared 8 months after the operation. In the fifth case, follow-up has been too short to permit evaluation of the results. Eight patients were subjected to the therapeutic procedure; five have suffered no further hemorrhage, two have been lost to follow-up, and in one the operation is too recent to be taken into account at present.

The excellence of these results suggests that surface diathermocoagulation may be recommended in the treatment of Eales' disease.

Comment: The successful surgical therapy of a progressive retinal disease deserves to be called to the attention of ophthalmologists. Improvements in methods of examination and diathermy application permit the precise localization and coagulation of retinal lesions. There is evidence from this report by Franceschetti, as well as reports by several other authors, that such diathermy can be successfully applied in Eales' disease.

One must not overlook, however, the recent reports of successful medical therapy of Eales' disease. In some instances this granulomatous periphlebitis can be attributed to tuberculosis and responds well to streptomycin, isoniazid, and PAS therapy. Other cases have been seen which had evidences of toxoplasmosis and which responded dramatically to daraprim and sulfadiazine therapy.

Successful applications of surface diathermy have been reported in recent years in the therapy of angiomatosis retinae and small malignant melanomas (particularly in one-eyed patients). The ingenious device described by Meyer-Schwickerath (Light-Coagulation: A new method for the treatment and prevention of retinal detachment. Acta XVII Concilium Ophth., 1954, 404) offers attractive possibilities for the treatment of such lesions. This method of coagulation by a focussed beam of light would permit the obliteration of such lesions as those seen in Eales' disease without any operative incision and without the extensive scleral necrosis that follows diathermy.

BERNARD BECKER

Basic Sciences

BACTERIOLOGY

TISSUE CULTURE TECHNIQUES IN THE STUDY OF HERPETIC INFECTIONS OF THE EYE

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Am. J. Ophth., 1955, *40:* 189–193

Improvements in tissue culture techniques during the past few years have advanced the study of virus diseases by making available more rapid diagnostic methods. Infections of the cornea caused by the viruses of herpes simplex, vaccinia, variola, and epidemic keratoconjunctivitis still present difficulties in diagnosis, but it now seems possible, through tissue culture methods, to differentiate these diseases by the laboratory investigation of eye washings.

An attempt has therefore been made to develop a more sensitive test for the virus of herpes simplex. Tissue cultures of rabbit corneal epithelium, the human carcinoma strain HeLa, and human kidney, which seem to be most advantageous in the isolation of the herpes simplex virus, were used in studying the changes produced by herpetic infection. Characteristic nuclear inclusions and giant cells were found in all the tissues within a few hours after infection with herpes-simplex virus strain H51, which was isolated from a patient showing central corneal ulceration and which has been maintained by intracerebral inoculation of adult mice.

Although tissue cultures of rabbit cornea, human kidney, and HeLa cells appeared to be equally susceptible to strain H51, attempts to isolate a virus from collected specimens were carried out using rabbit cornea because of the short time elapsing before this tissue showed the typical cytopathogenic changes. In a survey of 20 cases of suspected herpetic infection, it was found that specimens from 13 of them produced characteristic changes in tissue cultures of rabbit cornea (fig. 1). Eleven of the 20 cases were tested in parallel on the scarified cornea of a rabbit. In no instance were signs of infection evident in the rabbit eye without a corresponding change in the tissue culture. Of particular importance is the fact that, in three cases, characteristic changes were seen in inoculated cultures but not in the corresponding inoculated rabbits. Furthermore, a positive response could be readily detected in most unstained tissue cultures within 12 hours, and in stained preparations within 8 hours, whereas a positive reaction in the rabbit eye was not visible for at least 30 or 40 hours. A laboratory report, therefore, based on the findings in inoculated cultures was possible within about 12 hours after receipt of the specimen. A report based on the findings in inoculated rabbits

was not possible until after 7 to 10 days, because of the long histologic procedure required for the cornea in toto.

Experiments conducted to determine whether the agent isolated in the collected specimens was in fact the virus of herpes simplex clearly established its identity. Tissue culture fluids from positive cultures were put through four successive passages, resulting in the appearance of characteristic changes at each stage. Positive fluids were also passed to rabbits and suckling mice, resulting in each case in a recognized herpetic response.

The techniques used provide a relatively simple rapid method for the determination of herpetic antibody in human serum. Acute and convalescent phase sera from a number of patients from whom herpes-simplex virus had been isolated were tested in tissue cultures against the H51 strain. The neutralizing antibody

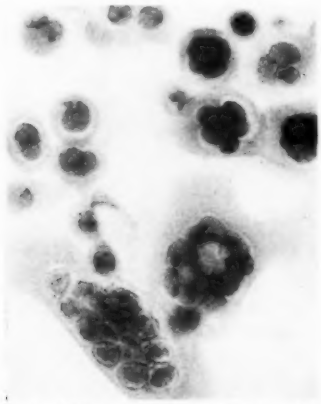

FIGURE 1. Tissue culture of rabbit cornea 20 hours after inoculation with washings from case of stomatitis. Note the giant cells containing clusters of nuclear inclusions. Hematoxylin and eosin. × 259. (Reproduced by the courtesy of the authors and the American Journal of Ophthalmology.)

level of these sera was demonstrated by their ability to neutralize the virus, thereby inhibiting the usual cytopathogenic changes seen in infected cultures.

These tissue culture techniques also provide a rapid diagnostic method, which is more sensitive than the standard method of rabbit cornea inoculation. Certain problems in the laboratory diagnosis of herpetic infections, however, still remain to be solved. For example, herpes-simplex virus was isolated from 9 of 10 specimens collected from patients with either stomatitis or skin lesions, whereas it was recovered from only 5 of 10 cases of keratitis. Some modification, therefore, may have to be made in the present method if it is to be used successfully in uncovering latent virus, or virus that has been rendered inactive by local antibody or the action of some undetermined process.

Comment: The need for a rapid diagnostic test for herpes simplex virus arises chiefly in cases of atypical dendritic keratitis, methaherpetic keratitis or, more rarely, in follicular

conjunctivitis of undetermined etiology. The test described by the authors requires the facilities of a research laboratory and will find its application chiefly as a research tool. In clinical practice it would be useful to have a sensitive test for the presence of herpes virus in order to avoid the administration of corticoids to such cases. Until the sensitivity of this test can be established such compounds should be withheld from all cases in which herpetic etiology is suspected on clinical grounds.

HENRY F. ALLEN

STUDIES OF IMMUNITY IN VACCINIA KERATITIS IN RABBITS

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Am. J. Ophth., 1955, *40:* 194–200

The importance of circulating antibodies in the development of corneal immunity to virus infections has been emphasized by various investigators. Vaccinia virus, which is especially suitable for use in immunologic studies because of its ability to stimulate antibody formation, was therefore used in an investigation designed to evaluate the degree of corneal immunity produced by various immunizing procedures. Rabbits were used as experimental animals and the course of corneal infection was followed by observation with a hand slit-lamp. The virus used for corneal vaccination was manufactured for immunization against smallpox. It is sealed in equal quantities in fine glass tubes, insuring an effective dose in each. Before vaccinia virus was placed on the cornea, local anesthesia was obtained with pontocaine and the epithelium was scratched with a needle. Virus used for intravenous injection was rabbit lapine, prepared from the crusts of 3-day-old vaccinia lesions. Serologic immunity was measured by the complement fixation reaction using the method outlined by Craigie and Wishart.

The experiments were carefully designed to show the effect on corneal immunity of (1) corneal vaccination, (2) corneal vascularization, (3) hyperimmunization, and (4) subconjunctival injections of vaccinia virus. Analysis of the findings obtained in the various groups of animals so tested showed that moderate levels of serum antibody to vaccinia virus were obtained after either skin or corneal inoculation, and that these levels were sufficient to confer a slight degree of resistance to a subsequent inoculation of the intact cornea. Vascularization of the cornea as a result of keratitis produced by injections of horse serum increased the resistance of the eye to the virus, but the degree of resistance thus obtained was not so great as that found after a previous corneal vaccination. Hyperimmunization of rabbits by intravenous injection of live vaccinia virus resulted in high serum antibody titers which produced a further modification of the corneal infec-

tion but did not give complete protection against the virus. Finally, the highest degree of corneal immunity was seen in eyes which had recently recovered from a vaccinial keratitis and in eyes which had received subconjunctival injections of virus.

The development of a high degree of corneal immunity following subconjunctival injections of virus may be another manifestation of the stimulation of local antibody formation, which is believed to be an important factor in the appearance of immunity after a recent vaccinia infection. Corneal immunity, however, has been produced by intracorneal injections of inactivated vaccinia virus and may, in this case, have been due to the interference phenomenon, since the effect was obtained before the development of immune bodies could have been expected. The difficulty of differentiating the interference phenomenon from a local immune response when immunologically related viruses are employed makes it unwise to draw definite conclusions in regard to the exact mechanism by which immunity is acquired after subconjunctival injections of virus.

If corneal immunity in man is similar to that in rabbits, dermal vaccination alone is not likely to result in complete protection of the cornea against variola and vaccinia infections. Subconjunctival injections of virus may, however, be of practical importance in immunizing corneas that are subject to recurrent virus infections.

Comment: The present study provides evidence complementary to previous studies of immunity to herpetic infection in rabbits by the Ormsby group and to clinical evidence from herpetic keratitis in humans. All of this indicates (1) that humoral antibodies modify but do not prevent viral keratitis in previously uninfected eyes of immune animals, (2) that local antibodies may prevent reinfection upon reinoculation of a recently infected eye, and (3) that the protective effect of these presumptive local antibodies tends to disappear in time. That the role of humoral antibodies in affecting established infection is a minor one is further suggested by the failure of human immune serum globulin administered either topically or systemically to modify the course of clinical cases of dendritic keratitis. This finding is consistent with the belief that circulating antibody does not penetrate intracellularly and the probability that the virus spreads from cell to cell of an epithelial layer without being exposed to extracellular antibody. Whatever protective effect the latter may have is presumably exerted before the virus has become "fixed" to the cells which it would otherwise infect. The role of corneal vascularity in modifying infection presumably depends on the concentration of circulating antibody at the site where extracellular virus would be exposed to its neutralizing effect.

If, as now appears, protection depends on the presence of local or tissue antibody, the problem of prevention of recurrent viral keratitis centers around maintaining such antibody at a consistently high level. It does not seem likely that this can be achieved by methods applicable in clinical practice.

HENRY F. ALLEN

BIOCHEMISTRY

CRITICISM OF THE DETURGESCENCE THEORY OF CORNEAL TRANSPARENCY

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AND

V. EVERETT KINSEY

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Acta XVII Concilium Ophth., 1954, 483–489

The cornea must be in a deturgescent state if it is to remain transparent. According to the earlier hypothesis proposed by the authors (Arch. Ophth., 1942, *28:* 661) there is a net movement of water from the anterior and posterior surfaces of the cornea as the result of osmotic forces. This selective movement requires the presence of semi-permeable membranes and a potential osmotic gradient between the tears and corneal stroma on the one hand and between the aqueous humor and the corneal stroma on the other. These somatic forces arise because the precorneal tear film and the aqueous humor are hypertonic to the interstitial fluid of the cornea. The fluid of the corneal stroma is considered as being in a steady state with the blood at the limbus and a net loss of water occurs at the surfaces of the cornea. No implication may be drawn concerning the relative amount of water passing through the epithelium and endothelium.

Criticism of the theory has arisen because of new observations, particularly with tracer elements, that have been interpreted as inconsistent with the theory. The demonstration of significant concentrations of enzyme in the epithelium and endothelium has suggested that these membranes operate in the active transport of fluid and not as passive semi-permeable membranes. The assumption that the enzyme activity is determined by the metabolic requirements of these membranes and not by an active secretory function is in keeping with the deturgescence theory.

Recent studies with tracer elements have indicated a relatively free permeability of the endothelium to sodium in both directions. It thus behaves not as a semipermeable membrane, but as a very leaky membrane having relatively free permeability. These results appear to be equally incompatible with the concept based on a semi-permeable property or that based on a secretory property of the endothelium.

Osmotic tensions of the aqueous humor have been compatible with the presented theory of deturgescence but objections have been raised on the basis that the osmotic tension of tears is not sufficiently hypertonic to the corneal fluid. The

dual responsibility of endothelium and epithelium in maintaining deturgescence, allowing one to compensate to some extent for the other, prevents corneal swelling even though the hypertoxicity of the tears is not continually maintained as in sleep.

In some conditions, none of which are physiologically significant, the cornea becomes opaque without swelling, as occurs with acids. This has no bearing on the normal physiology of the cornea.

It is concluded that with the possible exception of the "free" permeability of the endothelium to tracer electrolytes which requires further quantitation, there do not appear to be any major objections to the deturgescence theory as originally presented. The alternative proposals of vital activity or secretory processes on the part of the corneal endothelium or stromal cells have little to recommend them in the way of positive evidence and much against them in the way of negative evidence.

Comment: This paper is just one of an excellent series of papers given at the last International Congress on corneal transparency and its relationship to hydration and metabolism of the cornea. We have chosen to abstract the contribution by Cogan and Kinsey since it includes the critical comments made by other members of the symposium, in particular Dr. D. M. Langham of England and Dr. A. M. Potts of Cleveland.

Drs. Kinsey and Cogan first presented the so-called deturgescence theory of corneal transparency in 1942 as a result of *in vitro* experiments performed on excised corneas. An excellent presentation of the theory is given by Adler in his "Clinical Physiology of the Eye" (Mosby Co., 1950). In essence the cornea was considered a rather inert structure whose hydration (and therefore transparency) was controlled by osmotic forces acting internally and externally to it. An intact endothelium and epithelium maintained the proper concentration gradient.

Through the intervening years numerous objects have arisen to this theory. Some of them are merely quantitative (e.g., tonicity of tears) but others present formidable data. The chief among these is the independent finding by Potts, Davson and Langham that the endothelium *in vivo* is almost completely permeable to sodium. Dr. Kinsey answers this as best he can but it remains a thorn in the side of the osmotic theory. At this time only a compromise solution can be offered. The cornea is like tissues anywhere in the body and performs work: the necessary enzyme systems are well established. (Pau, H. Enzyme localization and corneal swelling. Deutsch. Ophthal. Gesellsc. 1953, p. 130–134) and the end result of this work is transparency. Conversely interference with the energy requirements of the cornea results in opacification. Whether the work performed is in the nature of a true pumping action as in the kidney or simply the maintenance of relatively "semipermeable membranes" remains to be seen.

DAVID SHOCH

COLOR VISION

CONGENITAL TOTAL COLOR-BLINDNESS

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Ghent, Belgium

Bull. Soc. Belg d'Ophtal., 1955, *110:* 170–254

The findings in some 430 cases of congenital total color-blindness reported in the literature, supplemented by those in three personally observed, show that the commonest form of this condition is complete congenital color-blindness with amblyopia, which was present in 240 of the patients. Incomplete congenital color-blindness with amblyopia, in which some perception of color persists, comes next with only 15 established cases, followed by congenital color-blindness without amblyopia, in which there is usually no color perception but vision is normal or only slightly diminished (14 cases). The two proved cases of unilateral congenital color-blindness found in the literature may be included in this last group. The hereditary character of complete congenital color-blindness with amblyopia, which is of the recessive autosomal type, is shown by the fact that 70 per cent of the 215 cases for which the data are adequate were familial and 30 per cent were nonfamilial—proportions very close to the 25 per cent and 75 per cent theoretically characteristic of a recessive autosomal affection.

The general condition of persons with total color-blindness is usually quite normal; concomitant bodily defects, if they exist, are due as a rule to other pathologic genes. Objective examination of the eye is often negative, but certain changes (discrete macular alterations or genuine macular degeneration, papillary pallor, and astigmatism) do appear with a frequency that makes it possible to consider them as real, though inconstant, symptoms of the affection. Ordinary ocular malformations and anomalies, such as pigmentary retinopathy, that are caused by pathologic genes of a different kind may also be found in these patients. The most significant functional change lies in the fact that the curve of spectral luminosity in photopic vision in patients with color-blindness is almost the same as that found in scotopic vision in normal subjects, and that Purkinje's phenomenon is therefore lacking. The central visual acuity is normal in scotopic vision and generally far below normal in photopic vision. In general descriptions, the vision is often regarded as always being reduced to about 0.1. In fact, it may it may be either better or worse. It often differs in the two eyes. Contrary to current opinion, only the visions that are above m plus 2 sigma (log 1.24, or about 0.5) and those that are below m minus 2 sigma (log 2.58, or about 0.08) should be considered abnormal.

It has long been known that the visual acuity of the total color blind depends on the ambient light, diminishing when the light exceeds a relatively low degree, whereas the visual acuity of normal subjects increases as the light increases up

to a very high luminance. Peripheral visual acuity regularly increases from the periphery to the paracentral region and is sometimes clearly higher than in the normal subject. The peripheral limits of the photopic visual field are almost always normal; the middle region is characterized by a pronounced disturbance of spatial summations; and a relative photopic central scotoma is present in some, but not all, cases.

The polymorphism of the condition is well illustrated by the diversity of the dark adaptation curves, which may belong to any of four essentially different types: low monophasic, high monophasic, low biphasic, and high biphasic. The high biphasic curves are the most frequent. The absolute threshold is generally normal. Contrary to what might be expected, the macular curves are usually biphasic with an infranormal absolute threshold. The peripheral thresholds of the scotopic visual field are normal; on the other hand, the central scotoma in the dark is generally less dense than in a normal subject and may even be absent. The differential thresholds in the authors' patients were clearly altered; in general, however, they have received little attention from investigators. The critical frequency of subjective fusion is normal at the scotopic level, but at the photopic level it is reduced to about half the value it has in the normal subject. In spite of their amblyopia, the authors' patients were able clearly to perceive Haidinger's brushes. Perception of Purkinje's after-images remains generally unchanged.

The resting retinal potential measured indirectly in the three patients by electro-oculography seemed to be normal; the electroretinograms showed a generally normal b wave, but the a wave was greatly reduced or absent and the critical frequency of objective fusion was lowered. Binocular vision is often weakened or lacking and strabismus is very often present. Nystagmus, which with photophobia is one of the most obvious symptoms of color-blindness, is essentially of the pendular type, analogous to that found in albinism and other ocular affections with congenitally poor vision. Characteristically, it tends to diminish or disappear with age, often in the second decade of life. The photophobia of color-blindness differs from that found in inflammatory conditions of the eye: the color-blind patient exposed to a bright light experiences, not pain, but a diminution of vision accompanied by a tendency, often irresistible, to protect himself against the excess of light. Study of pupillary changes shows that the size of the pupil in monochromatic light is proportional to the spectral luminosity. The photopic photomotor reflex is definitely altered in its mydriatic phase. Only one case of congenital color-blindness has become the subject of histological study: in it, the number and distribution of the cones was normal but the foveal and parafoveal cones were found to be deformed.

The authors' patients, a boy and two girls, were the only ones in their families to be affected. General examination was negative in the first and the third; the second showed electroencephalographic changes. All had a total absence of color perception and showed a characteristically altered spectral luminosity. Pseudophotophobia, nystagmus, and strabismus were also present in all, and one or all exhibited other abnormalities in varying degrees.

None of the theories advanced to explain the origin of typical total color-

blindness can be accepted without reserve. It is undoubtedly a functional anomaly and not a disturbance dependent upon the macular lesions. In the absence of proof to the contrary, it may be considered polymorphic.

Comment: This is by far the most extensive and astute digest of the literature of this condition, to date. If there is a weakness in the authors' treatment, it relates to the dark-adaptation curve—their own cases were too few (3!), and the techniques of others too various, for them to have much right to say that among total-color-blinds there are four distinct types of curve. Sloan, who did a good deal of work with each of her subjects, found only two types and was quite sure that the rapid monophasic type usually resulted from the subject's "cheating" during his highly unpleasant preliminary light-adaptation.

GORDON L. WALLS

Orbital Pneumotomography, which combines the retrobulbar injection of 10 to 15 cc. of air into the muscle cone with sectional radiography, not only aids in the demonstration of soft-tissue tumors in the retrobulbar space but also localizes and delineates their borders. The procedure, described in the literature by de Abreu of Brazil and various European authors, has been used successfully in the New York Hospital-Cornell Medical Center in 12 cases of unilateral exophthalmos in which a tumor was either suspected or had to be ruled out as a possibility. In two of the patients, well-demarcated abnormal soft-tissue masses were demonstrated in the pneumotomograms and proved at operation to be hemangiomas of the size and shape and in the position indicated in the films. Two other patients with unilateral exophthalmos were found on orbital pneumotomography to have soft-tissue tumors contiguous to the optic nerve. For the present, the patients are being followed, but the tumors, which are thought to be either optic-nerve or nerve-sheath tumors, will be removed surgically if necessary. In still another patient in this group of 12 the pneumotomograms showed no tumor. The exophthalmos, which had appeared rather suddenly, was therefore attributed to a pseudotumor and treatment with ACTH was instituted with a complete return to normal within two weeks. Surgical exploration in another patient—a 5-year-old child with unilateral exophthalmos—in whom no retrobulbar abnormality could be demonstrated by orbital pneumotomography revealed a fibrous-tissue mass in the anterior-superior medial portion of the orbit. With one possible exception, no tumor was found in the other cases. Orbital exploration without localization, which is often a traumatic and unproductive procedure, can be avoided in many cases by the use of orbital pneumotomography. Moreover, the exact localization obtained by this means when a tumor is present enables the surgeon to plan his surgical approach to the best advantage. W. Dubilier, Jr., H. von Gal, A. Freemond, and J. A. Evans, the Department of Radiology and Section of Ophthalmology of the Department of Surgery, the New York Hospital-Cornell Medical Center, New York, New York, Radiology, 1956, 66: 387–392.

GENETICS

THE VALUE OF HEREDITY IN THE DETECTION AND STUDY OF GLAUCOMA

Leo Kellerman and Adolph Posner

New York, N. Y.

Acta XVII Concilium Ophth., 1954, 1129–35

A positive family history of glaucoma was obtained in 13.5 per cent of 199 patients with primary glaucoma. One hundred ninety-two of their relatives were examined and eight (or 4.16 per cent) were found to have definite primary glaucoma. All were of the chronic simple type. Eleven (or 5.7 per cent) were considered borderline cases. None of the discovered cases had any awareness of disease in the eyes and all but one were in a very early stage of glaucoma. The incidence of glaucoma in unselected samples of the general adult population has been variously estimated at .5 to 2 per cent.

These results show that for purposes of glaucoma case finding, the relatives of glaucoma patients constitute a group with a high incidence of unsuspected glaucoma. Of a total of 257 pedigrees obtained, 34 were found in which the glaucoma seemed to be transmitted in a dominant form. Within members of the same family, there was a tendency towards similarity in the width of the filtration angle. This suggested that the angle width may be an inherited anatomic feature which is of special significance in the case of narrow angle glaucoma. If borne out on larger samples, this observation will strengthen the concept that chronic simple glaucoma and narrow angle glaucoma are separate diseases, both clinically and genetically.

CLINICAL CONSIDERATIONS CONCERNING THE HEREDITY OF GLAUCOMAS

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Bull. Soc. Belge d'Ophtal., 1955, *110:* 255–266

Most of the studies dealing with the heredity of glaucomas are intended to add to our knowledge of genetics. In fact, however, studies of this kind have great practical importance, because they may lead to the discovery of unsuspected cases, provide information about incipient forms of the disease, help to identify

atypical forms, and aid in the solution of the many problems still unsolved. Consequently, the routine examination of a patient with glaucoma should always include, not only the drawing up of his genealogical tree, but also in so far as possible an investigation of his ancestors, collaterals, and descendants.

This method was used at the Ophthalmological Service of the University of Liège in studying 162 families, at least one member of which suffered from one of the following forms of glaucoma: open angle glaucoma (87), closed angle glaucoma (61), and capsular glaucoma (14). The 87 patients with open angle glaucoma came from 87 different families. In 20 of these, investigation revealed the existence of 36 additional cases of glaucoma (24 certain and 12 probable). The familial glaucoma was demonstrated only in a single generation, i.e., in the patient's brothers or sisters, in 12 of the 20 families; in the other 8, it appeared in several generations.

Study of the families of the patients with closed-angle glaucoma showed 8 instances in which the condition was familial, with a total of 7 certain cases and 5 that were probable. Closed-angle glaucoma progresses by crises; between attacks, the diagnosis cannot be established or disproved by examination.

No familial cases of capsular glaucoma were found among the members of the 14 families studied; the investigation, however, should be pursused in larger series.

Three points of special interest were stressed in this study: (1) the symptoms of beginning glaucoma; (2) the characteristics of the disease in the different members of a single family; and (3) the possible coexistence of other ocular conditions. The initial symptom was found to be increased resistance to the flow of aqueous, of which the increase in the ocular pressure is a natural consequence. In most cases, the character of the disease was the same in all the affected members of a single family; if one member had open-angle glaucoma, his affected brothers and sisters had it too. The oldest members of a family line almost always present the most advanced glaucoma. Furthermore, the condition seems to begin at the sme age in members of the same generation.

The possibility of a primary vascular change in open-angle glaucoma is suggested by the frequent occurrence of retinal vascular lesions in patients with this condition. Such combinations occur too often to be mere coincidences.

Narrowness of the iridocorneal angle is the essential cause of the hypertension in closed-angle glaucoma and, when present, may serve as a basis for a presumptive diagnosis. This characteristic is influenced by genetic factors, as well as by the patient's age and sex.

The fact that open-angle glaucoma was found to be familial in some families and closed-angle glaucoma in others supports the belief that these two conditions are separate entities.

Comment: This editor has long stressed the fact that mass screening methods for the detection of glaucoma would have been more profitably applied to a careful survey of the relatives of known glaucoma patients. A most potential fruitful source of material is our *large glaucoma clinics.*

In these articles statistical confirmation of the value of such a study performed on the relatives of known glaucoma patients is presented. A rewarding by-product of the authors'

study was the observation that an anatomical narrow angle may be hereditarily determined.

Every ophthalmologist should feel it his professional responsibility to inform his glaucoma patients of the possible hereditary nature of their disease and urge that their relatives seek ophthalmological examination.

HAROLD F. FALLS

A NEW SYNDROME ASSOCIATED WITH ARACHNODACTYLY

BERNARD KRONENBERG

New York, New York

Acta XVII Concilium Ophth., 1954, 579–584

A pedigree of a new syndrome consisting of arachnodactyly, ptosis and pseudo-pannus is described. The pseudo-pannus consists of epithelium growing in all around the cornea but more marked above and below leaving an oval-shape of clear corneal epithelium centrally. Vascular loops continue from the limbus into the abnormal epithelium.

The description of arachnodactyly and its associated deformities such as kyphosis, scoliosis, funnel-chest, pigeon-breast, and other changes such as cardiac anomalies, anomalies in the size of the head and ears have been summarized by Rados (Arch. Ophth. 1942, *27:* 477). The most common ocular anomaly is a bilateral dislocation of the lenses. Of the 204 patients studied by Rados—101 males and 103 females—163 had ocular anomalies. Of these, 124 had dislocation of the lens or iridodonesis in a typical or atypical form. The remaining 39 had other ocular anomalies such as shallow anterior chamber, miosis, and strabismus. None of the cases reported by him showed the ocular signs reported here.

A pedigree chart of 54 members of the family in four generations was prepared. Thirty-two members were affected—15 females and 17 males. Transmission appeared to be dominant and was assumed to be due to a single chromosome.

Comment: Dr. Kronenberg's report lends further credence to the frequent clinical observation that the gene determining Marfan's syndrome is indeed most protean in its expressivity. Particular familial and individual variation (such as ptosis and corneal pannus in this family) presumably depends upon the gene milieu (the genotype) of that specific strain.

A similar pannus formation (the editor assumes in light of the absence of illustration) has been personally observed in a vast majority of cases of aniridia. The association of glaucoma with this pannus in aniridia suggests that the observed anomaly of the chamber angle is the common precursor of both. It is suggested (with tongue in cheek since Kronenberg did not record gonioscopic findings) that an anterior chamber defect may exist in the family reported by him.

HAROLD F. FALLS

OPTICS

STUDIES IN SPACE PERCEPTION

PAUL BOEDER

Southbridge, Massachusetts

Acta XVII Concilium Ophth., 1954, 188–192

An enormous amount of work has been done in investigating specific characteristics of the visual space, such as the horopter, stereopsis, and size constancy. However, a general characterization of an individual's visual space in relation to the physical space has not been attempted. It is suspected that there are significant differences between the visual spaces of a myope and a hypermetrope and that the world of a child differs from that of an adult.

Ames constructed a set of rooms, one of rectangular shape, others with curved walls and correspondingly distorted window frames. The distorted rooms were constructed so that the binocular retinal imagery arising from them was the same as that produced by the rectangular room. If viewed from the proper station points, all rooms have the appearance of rectangular rooms. Presumably they do not appear distorted because the experience of living in rectangular rooms causes the individual to see the rectangular form even when the physical counterpart has marked curvatures. The experiment proved that perception is not merely dependent on the physiological stimulus-pattern but also on the observer's "choice" from among an infinity of possible external configurations, a choice which in turn depends on the purposes, the past experiences, and the expectations of the observer.

Luneburg (J. Optical Soc. Amer. 1950, *40:* 627) observed that there is not a complete lawlessness in visual space. For instance, Ames' distorted rooms cannot be constructed arbitrarily; certain metric clues must be identical in all of them. Thus, visual perceptions are not merely the chance result of psychological conditions, but are governed by certain constant, non-psychological factors which, though not determining the perception completely, play an integral part in its formation.

Luneburg determined experimentally that comparative size sensations are determined by the physical coordinates of the object points although sensory inequalities do not necessarily correspond to the physical inequalities. These observations form the basis for Luneburg's hypothesis that binocular visual space can be described as a measurable or metric mathematical space.

Once it is accepted that sensory relations of distance are not the same as physical relations, it is clear that the metric space of binocular vision may have properties quite unlike those of physical space. For instance, a curved physical configuration will generally be sensed as straight conversely, physically straight lines usually appear curved to the observer. In establishing the relation between

visual and physical space Luneburg related then to the Vieth-Muller circle. This is a circle lying in the horizontal plane and passing through the centers of rotation of the eyes, with its points, therefore, points of equal convergence-demand.

Blank (J. Optical Soc. Amer. 1953, *43:* 717) somewhat simplified Luneburg's theory by showing that perceived distance is a function of the difference of convergence angles associated with physical points under consideration. This function completely characterizes the visual space of an individual. When it has been found it is possible to predict the quality of judgment concerning straightness, angles, relative size, in short, the geometry of his visual space.

The experimental work of Handy (Geometry of Binocular Space Perception, 1953) provided strong evidence that it is possible to determine experimentally the metric that completely characterizes an observer's binocular visual space, much as his color matrix describes his sense of hue and saturation.

Comment: Dr. Boeder has performed a great service by bringing this material to the attention of an international audience. It is a dramatic, and an essentially American story he reveals. Unforunately, all the three great protagonists of this story are now dead. Ames and Hardy were American-born and educated and Luneburg, a German-born mathematician, also brought his genius to its (alas, much too brief) flowering in this country. Ames' thinking, in the last years of his life, crystallized in a transactional, essentially utilitarian-psychologic, viewpoint. At the same time, his numerous beautiful and ingenious experiments on space perception demonstrated most convincingly that nothing in this field is as important for the final perceptive response as the configuration of the retinal stimulus pattern itself. Ames' work was the fertilizing ferment for Luneburg's concept and Hardy brought the viewpoint of the ophthalmologist and the teamwork of a great institution into the service of these ideas. While Ames' work is beguiling with great simplicity, that of the latter two authors is entirely esoteric to those mathematically uneducated and more than frustrating to those mathematically unsophisticated. Even Dr. Boeder, one of the most eminent popularizers of optical mathematics for the ophthalmologist, cannot expect to make Luneburg's theses and Hardy's studies clear. Thus, it is hoped that through his publication in the ACTA and this short review of his paper others will be made aware of an important development in the study of space perception.

ARTHUR LINKSZ

THERAPEUTICS

AN EXPERIMENTAL CLINICAL EVALUATION OF DORSACAINE HYDROCHLORIDE (BENOXINATE NOVESINE)

RICHARD EMMERICH, GEORGE Z. CARTER AND CONRAD BERENS

New York, New York

Am. J. Ophth., 1955, *40:* 841–848

The subjective reactions of 408 patients to the instillation of Dorsacaine (0.4 per cent) was significantly less than those following the administration of Pontocaine (0.5 per cent). Subjective irritation was directly proportional to the concentration and larger drops produced a more intense sensation of stinging than small. The sensation was significantly less when the medicated eye was kept closed after the instillation of the drug.

Dorsacaine caused a more rapid onset of surface anesthesia than Pontocaine solution. The duration of anesthesia following the instillation of Dorsacaine was slightly less (average 18.0 minutes) than with Pontocaine (average 21.3 minutes).

Systemic toxicity was not encountered following the topical application of either Dorsacaine or Pontocaine into the conjunctival sac. Macroscopic observation of over 600 eyes revealed that hyperemia occurred in 26 eyes following medication with Dorsacaine, whereas 57 of the Pontocaine-treated eyes became injected.

The microscopic changes in the corneal epithelium were significantly less after the application of Dorsacaine than after the use of Pontocaine. Dorsacaine had no essential effect on pupillary size or reactions, tension, and accommodation.

Comment: It is interesting that careful investigators working with the same drugs but employing different techniques can come to somewhat different conclusions. Emmerich and his co-workers feel that Dorsacaine is decidely more rapid in action than Pontocaine (tetracaine); of shorter duration and less irritating. Linn and Vey (Am. J. Ophth., 1955, *40:* 697) were not able to demonstrate any significant difference between the two agents. The difference in conclusions can probably be attributed to the difference in techniques employed in the studies. Regardless, it appears that Dorsacaine is a safe local anesthetic in 0.4 per cent solution for ophthalmic use.

IRVING H. LEOPOLD

THE CONTRAINDICATIONS OF VASOCONSTRICTOR DRUGS IN OPHTHALMOLOGY

GIANLUIGI COLOMBO

Milan, Italy

Acta XVII Concilium Ophth. 1954, 325–6

Naphthetylimidazolin has the following advantages in ophthalmology: it does not change in solution (like epinephrine); it can be mixed with other drugs such as atropine, pilocarpine, etc. without inconvenience. It is used extensively not only in prescriptions but also by women who like to constrict the blood vessels of the bulbar conjunctiva.

In conjunctivitis (infectious types) the reduction of blood circulation given by imidazoline reduces the defense of the tissue against the infection and decreases the efficiency of antimicrobical substances instilled thus prolonging the disease. For the above reasons, imidazoline is not to be used against mixed conjunctivitis or with antibacterial substances. Imidazoline can be successfully used in spring catarrh and in allergic conjunctivitis as well as in other ocular disorders in which it is sometimes therapeutically useful, especially for epiphora, because vasoconstriction in the naso-lacrimal mucous membranes enlarges the lacrimal channels.

Comment: Dr. Colombo has pointed out that vasoconstrictor agents have a definite place in local therapy in ophthalmology. They are valuable in allergic varieties of conjunctivitis, in aiding in the control of a partially blocked naso-lacrimal apparatus, for dilatation of the pupil and for aid in the control of intraocular pressure in properly selected cases. He has properly stressed that the use of this agent for cosmetic purposes such as to produce a pale bulbar conjunctiva must not be overdone. There is a possibility that the vasoconstrictor drugs, by their repeated use, may lead to reactive dilatation and actually increase the apparent hyperemia eventually. In addition, he properly states on theoretic grounds that vasoconstrictors will reduce the blood flow in the conjunctiva and therefore decrease the ability of the tissues to overcome infection.

IRVING H. LEOPOLD

LONG-TERM ADMINISTRATION OF ACETAZOLEAMIDE (DIAMOX) IN THE TREATMENT OF GLAUCOMA

CARL KUPFER, CARTERET LAWRENCE AND ERIK LINNER

The Wilmer Ophthalmological Institute of the Johns Hopkins University and Hospital, Baltimore, Maryland

Am. J. Ophth., 1955, *40:* 673–685

A group of 29 patients with advanced glaucoma of different types were given long-term treatment with Diamox and miotics. Twenty of these were treated

an average of 10 and a half months with Diamox. Of these, 12 were classed as being under good control, six as under fair control, and two as under poor control. Of the remaining nine, five patients required surgery before the close of the study, two patients developed scotomas (one with visible macular change) while under Diamox therapy, and two patients discontinued the drug because of shortness of breath and weakness. Two patients developed a late resistance to Diamox treatment.

It is felt that the long-term use of Diamox can be a useful adjunct in the treatment of advanced glaucoma. There remains the possibility that significant complications will be revealed by a larger series of patients and by a longer period of treatment.

Comment: The findings of Kupfer, Laurence and Linner are essentially similar to those of Becker and Middleton who found that 62 per cent of 50 patients with open-angle glaucoma uncontrolled by miotics were adequately controlled for 6 to 15 months when Diamox was added to their therapy. Two-thirds of the failures resulted from intolerable side-effects. Six per cent of the 50 patients developed true resistance to Diamox.

It is apparent from all reports to date that Diamox does not cause any complications in the lens or retina during the course of therapy. This is believed to be due to the ability of the eye to continue secreting aqueous at about 40 per cent of its usual rate, even in the absence of carbonic anhydrase.

H. Saul Sugar

It has been known since 1941 that a variety of sulfonamide derivatives are effective as hypoglycemic agents in animals. Recent reports have shown that the sulfonylureas are effective in eliminating the need for exogenous insulin in many adult patients with diabetes mellitus. Tolylsulfonylurea was administered to forty-four diabetics and a hypoglycemic response occurred in thirty-four. The ten subjects who did not respond developed the metabolic disorder before the age of 20 years and had the syndrome for 8 to 30 years. The data support the hypothesis that the insulin insufficiency of the majority of patients with diabetes mellitus is due to an increase in the rate of destruction of insulin by the tissues rather than to a marked decrease in the rate of production of insulin by a severely damaged pancreas. Thus, the tolylsulfonylurea, acting as an insulinase inhibitor, may produce a decrease in the destruction of endogenous insulin with a consequent increase in the availability of insulin. The lack of response of patients in whom the metabolic disorder began in childhood and in whom it persisted for many years may be due to exhaustion of the pancreas such as occurs in animals that are chronically exposed to increased demands for insulin by the peripheral tissues. Mirsky, I. Arthur, Diengott, Daniel, and Dolger, Henry, Department of Clinical Science, School of Medicine, University of Pittsburgh, Pittsburgh, Pennsylvania, Science 1956, 123: 583–584.

Classics of Ophthalmology
JAMES E. LEBENSOHN, *Editor*

DIFFRACTION OF LIGHT

FRANCESCO MARIA GRIMALDI, S.J.

Physicomathesis de Lumine, Coloribus et Iride, 1665

(Extract based on translation by W. F. Magie: A Source Book in Physics, New York, McGraw-Hill, 1935)

PROPOSITION I

Light is propagated or diffused not only directly, by refraction, and by reflection, but also in still a fourth way, by diffraction.

First Experiment

A very small hole is made in a window shutter and through it the sun-light from a very clear sky is admitted into a room which is otherwise closed so as to be dark. The diffusion of this light will be in a cone or what is nearly a cone, and becomes visible if the air is filled with dust or if some smoke is set up in it. In this cone there is placed an opaque body at a great distance from the hole, and so that at least one end of the opaque body is illuminated. Then the before mentioned cone is received on a white board or on a sheet of white paper laid on the floor, and there is seen its illuminated base with the shadow cast by the opaque body which has been placed in the cone.

What should be especially noticed is that the shadow appears considerably larger in fact than it ought to be, if the whole thing is supposed to act by straight lines.

In addition, at its sides there is some color, always bluish at the side which is nearer the shadow and reddish on the further side. These bright bands apparently depend on the size of the hole because they are not seen if it is very large.

It may further be observed of the before mentioned bands of colored light, that the first is wider than the second, and the second is wider than the third (it has never yet happened that more than three have been seen). These decrease in the intensity of the light and of the colors in the same order in which they recede from the shadow. Yet the individual bands are wider and further apart, the further the white board on which they are received is from the opaque body casting the shadows, and further also by how much the more this is set obliquely to the solar radiation. This reason itself demands, because they are made by the rays which are part of the luminous cone and which become more and more separated from one another the further they proceed.

There may be someone perhaps who, because of his failure to consider this observation, is unwilling to recognize that the before mentioned bands are bands

of light, as we have said they are, but will contend that they sould rather be called bands of shadow, because he has not paid enough attention to those obscure colors which we have said appear at the sides of these light bands.

Second Experiment

An opening is made, perhaps a finger breadth wide, in the window shutter of a well darkened room, and in this opening is placed a thin opaque plate and through a very narrow opening in this plate sunlight is admitted and forms a cone of light. At a great distance from the plate another plate is placed so as to cut this cone at right angles. In it there is also a small hole through which some of the before mentioned cone of light, which is interrupted by the plate, is admitted. This plate is so placed that the base of the cone considerably exceeds the size of the hole, so that the hole is all lighted or filled with light. Then the light which enters through the hole will again form a cone or almost a cone. When this is cut orthogonally or is terminated by a smooth white surface it will show on this surface an illuminated base, notably greater than the rays would make which are transmitted in straight lines through the two holes.

For the experiment to succeed there should be bright sunlight because, as has been said, the holes should be very small, especially the first one, and also the white surface on which the base is received should be at a great distance from the hole, otherwise the base observed is either not at all or only a little larger than the base deduced by calculation.

Further it should not be omitted that the illuminated base appears in the middle suffused with pure light, and at either extremity its light is colored, partly reddish, partly also strongly bluish.

Editorial comment: "The discovery of diffraction and its successful mathematical analysis became most important arguments in favor of the wave theory of light. Light can be diffracted, meaning 'broken away' from its rectilinear path" (Linksz). Diffraction is a fundamental property of light, though not apparent when the wave front is relatively unrestricted. The image of a point is always a diffraction disk, which in contrast to other aberrations decreases in diameter as the size of the aperture increases. Hence, for the best visual acuity the pupil must be neither too small nor too large. For pupillary diameters between 3 and 5 mm. the resolving power of the eye is fairly constant.

The mathematics of the diffraction pattern was investigated by R. Airy in 1834. The central disk receives 84 per cent of the energy transmitted and the successive rings receive 7, 3, 1.5 and 1 per cent respectively. The diffraction patterns of the different waves of white light are superposed and the resultant image is characterized by variously colored rings. Because the threshold of the light-adapted eye is so high the rings of the diffraction pattern do not register and their overlapping is ignored. The situation is otherwise in dark adaptation and the increased sensitivity then present is consequently detrimental to the perception of fine detail.

Under proper circumstances certain structures of the eye can act as a diffraction grating and induce a diffraction spectrum seen as halos. When a normal eye observes a small bright source in dark surroundings a physiological halo is perceived produced by the radial structure of the crystalline lens. In such halos the angular diameter of the outer red ring is about 7°. The large halos produced by mucus on the corneal surface,—

with a diameter up to 14°,—is due to the distance of this source from the retina. Edema of the deeper layers of the corneal epithelium, as occur in acute glaucoma and photophthalmia, gives rise to vivid halos. The size of a glaucomatous halo varies from 7° to 12°, presumably because the edematous globules formed vary in size as the attack progresses, small droplets producing larger halos.

If parallel lines are etched closely on glass the rulings absorb the rays while the very narrow strips of unscratched glass allow the light to pass through. With white light this grating produces a diffraction spectrum in which the colors are uniformly distributed according to the difference in wave length, while in a prismatic spectrum the longer waves are crowded and the shorter waves are spread out.

No microscope can resolve details that are closer together than one-third of a wavelength of light because of the overlapping of diffraction disks from adjacent elements. With ordinary light this limit of resolution is realized with a magnifying power of 800, with which an eye having an acuity of 20/20 can just distinguish an interval of 0.19 micron. In microphotography using ultra-violet light of 275 millimicrons the resolving power is nearly double.

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BIOGRAPHICAL NOTE

Francesco Maria Grimaldi (1613–1662) was born and died in Bologna, Italy. In 1632 he became a Jesuit and for 25 years taught literature and mathematics. His chief interest, however, was in natural science. He made a chart of the moon and we owe to him much of the lunar nomenclature. With Newton and Huygens he inaugurated the first great era in the study of light. He first described and named the phenomenon of diffraction in a 16-page brochure that was published posthumously in 1665,—three years after Grimaldi's death. Robert Hooke, in 1672, independently communicated similar observations to the Royal Society of London. More than a century elapsed before it was realized that the strongest possible argument for the wave theory of light lay in this discovery.

Reports from Abroad

PAKISTAN

Partition of India into Pakistan and Bharat in August, 1947 created a vacuum in the medical field in general medicine and the specialities in particular, to which ophthalmology was no exception. Before partition the majority of doctors were nonmuslims (either Hindus, Sikhs or British) both among the specialists as well as the general practitioners.

Mass migration of people from across the border brought in its wake many liabilities but few assets, and the medical profession was among those which suffered the most. As a result it was difficult to find the necessary staff for the only recognised medical institution left to us at that time, namely King Edward Medical College, Lahore.

Incidentally, it may be mentioned here that in Pakistan there is no separate institute of ophthalmology with a full pathologist or research unit attached; there are only eye wards in general hospitals. Because of the small number of Pakistani ophthalmologists we have neither a separate ophthalmic association nor a journal of our own so far.

In addition to the wards in general hospitals the eye work is also carried out in various "Eye Centers" and "Seasonal Camps." Both of these are active during the months of February to April and September to November each year. The extremes of temperature combined with lack of air-conditioning necessitates these arrangements. Sweltering heat, with plenty of flies, puts the doctor on his guard in summer while the biting cold of late December and early January keeps the patients away from the hospital.

The most common eye ailments are trachoma and its complications and cataract. The "Eye Centres" and "Seasonal Camps" mainly cater to these, although glaucoma is the exception, as it has to be tackled wherever it is met with. Tumbling is the favorite operation for cataract.

In the regular hospitals which are yet few and widely separated (though since partition five new medical colleges and two medical schools have come into being which points toward a gradual and encouraging improvement in the existing state of affairs) and not properly equipped, the most skilled operative procedures such as keratoplasty, dachryocystorhinostomy* and operations for the detachment of the retina such as scleral resection etc., are being attempted with fair amount of success. The pity is we cannot accommodate all ophthalmic patients requiring medical attention in these hospitals. Ignorance and illiteracy together with ill-informed religious prejudices constitute our tragic handicaps in securing

* In Mayo Hospital (attached to King Edward Medical College, Lahore) a modified technique of suturing sac with nasal mucous membrane, as suggested by Prof. R. A. Syed, is being employed with good results.

cadaver corneas for keratoplasty. Hence the series is still small. Squint surgery which was not practiced much before the partition of the country is nevertheless being attempted much oftener now but with a handicap since orthoptists and orthoptic facilities are non-existent.

Our military counterparts, however, with better means at their disposal are going ahead with research work and have contributed original articles on trachoma, spring catarrh, allergic conjunctivitis, squint etc. to both local and foreign medical journals, while one on the normal intraocular pressure in this part of the world will be published soon.

Stable economic conditions are a great contributing factor in every advancement in any part of the world; we are handicapped by the lack of proper equipment and library facilities from pursuing patient research work because of paucity of funds.

Contact lens clinics are unheard of over here and the rather rare artificial eye service is far from being satisfactory. Institutes for the blind are a drop in the ocean, with the result that a majority of the handicapped are forced to beg in the streets for their livelihood.

The inadequacy of the service offered to those needing proper medical attention in this field by the few existing hospitals can be gauged from the fact that we have not been able so far to get rid of the quacks (locally known as "Ráwals"). They perform the couching operation in far flung villages and keep on shifting their "clinics" seasonally.

It might be of interest to point out that there are few cases of intraocular foreign body, demyelinating diseases, squint and uveitis, while acne rosacia and retrolental fibroplasia are scarce if found at all. The acrylic lens replacement operation is not favored and buried implants after enucleation are not done because of unavailability of material.

In spite of our handicaps, initial disadvantages and financial limitations we have made and are making headway in a gratifying fashion. We have abundant clinical material and almost missionary zeal for working in ophthalmology in Pakistan.

R. MUMTAZ
Lahore, West Pakistan

GREECE

For years the operation of dacryocystorhinostomy for the treatment of purulent dacryocystitis, a common disease in Greece, has been carried out after the Dupuy-Dutemps method, with great success. This operative method, however, is not completely satisfactory, because the excision of the bone, by means of a hammer and chisel is very unpleasant for the patient.

The ideal method for ostectomy would be entirely painless, not unpleasant for the patient, quick, and free of the danger of traumatic effects upon the nasal mucous membrane and should be available to every ophthalmologist.

Having this in mind, we applied the "Airbrasive Technique" using an "Airdent" unit (S. S. White Dental Mfg. Co) for the excision of the bone in one case, in which the bone was known, from a previous operation on the other side, to be unusually thick.

Through a small,wear-resistant nozzle, a stream of fine, hard abrasive aluminium oxide powder mixed in CO_2 is ejected at a pressure of 60 pounds. The effect of the high velocity stream of abrasive particles is a rapid cutting away of the bone against which it is directed, as if with a knife. The abrasive powder is effective in cutting bones only, and does not affect soft tissues.

The ostectomy carried out by this method was complete, the portion of the bone being removed with all its edges smooth. When the abrasive powder reached the mucous membrane in the nose, the patient had the feeling of a sting, which was helpful in finding out when exactly the powder cut through the bone.

After the ostectomy, there were no traumatic effects observed upon the mucous membrane. The lacrimal sac was well protected, but it proved impossible to excise the lacrimal crest.

The powder was washed away and the operation was completed in the usual way. On the second day after the operation, the wound showed a slight suppuration. Large doses of penicillin were injected and the lacrimal apparatus was washed with a penicillin solution. Ten days later the wound was completely healed and the operation was successful.

The "Airdent" Unit, as constructed for dentists, presents certain disadvantages. The complication of suppuration points is one of them. This may have been due to two causes: (1) from the moment the cutting began, the operation was no longer aseptic; (2) the tissues at the edges of the wound were traumatized by the abrasive stream. We believe both defects can be done away with by sterilizing the powder and protecting the tissues in some way, so that the apparatus, suitably modified, may be used for the purposes of ophthalmic surgery.

Thanks are due to Mr Leonidas Pisiotis, dentist, for the loan of the apparatus and assistance given.

D. J. Polychronakos
Thessaloniki, Greece

AUSTRALIA

Medical practice in the Commonwealth of Australia is under the jurisdiction of the States, New South Wales, Victoria, Queensland, South Australia, Western Australia and Tasmania with the exception of the Federal Capital Territory controlled by the Federal Government. Although the rights of the States are jealously guarded, matters affecting the Commonwealth as a whole, such as defence, quarantine and customs, are left to the Federal Authority. The institution of a National Health Service was decided in 1947 by a Federal Referendum. At the present time the National Health Service is based on a scheme of insurance and fee-for-service and was specifically designed to continue the system of private practice.

Four medical schools in the University of Melbourne, Sydney, Adelaide and Queensland supply the majority of medical practitioners in Australia. The University of Western Australia is in the process of forming another medical school. Registration of the medical practitioners is a matter for the State authority exercised through a Medical Board appointed by the Government of the State. The Board is empowered to register graduates of its own medical school and those British or foreign medical schools with which reciprocity has been established. This latter point is often unappreciated by the lay public and the press (perhaps deliberately by the latter!) with the result that the refusal of the Medical Board to register any individual who waves a medical diploma in its face is at once attributed to the wicked machinations of the British Medical Association.

Post Graduate Diplomas in Ophthalmology have been instituted by the Universities of Melbourne and Sydney. A course of instruction for post graduates wishing to take these diplomas is provided by the University of Melbourne and Sydney acting in collaboration with the Ophthalmology Society of Australia. Candidates may not take the second part of the examination before satisfying the Board of Examiners that they have had adequate experience not only in ophthalmology but also in general medicine and surgery. These courses attract candidates from the neighbouring countries of the South West Pacific as well as from Australia.

After examination at a higher level than that of the University diplomas, the Royal Australian College of Surgeons admits Ophthalmologists as Fellows. The Fellowship is highly prized as it carries more weight for a hospital appointment than either of the diplomas.

The Victorian Eye and Ear Hospital, Melbourne is the only public eye hospital in Australia. In the other states the need is met with large eye departments attached to the General Public Hospitals, the corresponding departments in Melbourne being smaller. The recent appointment of Dr. C. H. Greer from the London Institute of Ophthalmology as special pathologist to the Victorian Eye and Ear Hospital is a definite step forward and Melbourne hopes in time to have its own research institute.

The Ophthalmological Society of Australia was founded in 1939, the inaugural meeting being held at the Royal Australasian College of Surgeons in Melbourne. This was, in effect, the amalgamation of the States Societies under the aegis of the British Medical Association. With the exception of the war years, Congresses have been held annually in rotation, in the capital cities of each State.

The transactions of the Society are published annually and form a record of its growth. It is the custom to invite guests from overseas to each Congress. Unofficial visitors are welcome and the Congress gives them an opportunity of visiting Australia and receiving a warm welcome at a season chosen to show the country at its best.

In the years that he has been practising as an ophthalmologist, the writer has seen a definite progress in his speciality in Australia. Whilst there is a tendency to sneer at the out-break of "diplomatosis," there is no doubt that the programme set to the candidate for the diplomas has produced a more highly qualified and competent ophthalmic surgeon. The benefit of this is seen throughout Australia, a land of vast distances with a sparse population. Competently trained ophthalmic surgeons are to be found in the distant towns of the "outback" and no longer is it necessary to travel hundreds of miles to obtain skilled attention to the eyes either at a public hospital or in the rooms of a private practitioner. In addition, Melbourne and Sydney provide a Medical Eye Service to cater to the needs of the intermediate patient.

To demonstrate that its interests are not entirely parochial, Australian ophthalmology makes an occasional worthwhile contribution to the literature overseas.

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Book Reviews

Les Anévrysmes Artériels Intracraniens; Formes Anatomo-Cliniques, Signes Ophthalmologiques. By PAUL BONNET, Professor of Clinical Ophthalmology, The Faculty of Medicine of Lyon. Masson et Cie, Paris. Paper, 118 pp., 48 illustrations, 1,500 francs, 1955.

The stated purpose of this monograph is to draw to the attention of ophthalmologists the pertinent facts regarding arterial aneurysms of the circle of Willis and its tributaries, the internal carotids and the basilar with the two vertebral arteries, and to present to them the ocular signs which may be used to localize the anatomic changes. The author has covered the literature on the subject thoroughly and has used an occasional case of his own to point up the discussion. Figures have been adopted from many sources and are correlated well with the discussion. The bibliography is comprehensive.

After a brief review of the historical background and a description of the basic vascular anatomy, Dr. Bonnet discusses the relative frequency of such lesions, about one aneurysm in 100 routine autopsies, and quotes Poppen's well-known statement that an interest in aneurysms leads to more diagnoses. Females are slightly more affected than males. Although most cases are over 20 years of age, and over half are found after the age of forty, the author quotes several examples of such lesions in infants and children, one in a 2-month-old infant with a midline aneurysm and resultant hydrocephalus. Using the literature he reviews location and multiplicity of lesions—four out of five are located at the carotid end of the circle of Willis, the other at the vertebral end—a worthwhile fact in view of possible surgical approaches. He notes the associated anomalies of the circle of Willis, coarctation of the aorta, and polycystic kidneys, pointing out that these are the same anomalies one finds associated with von Hippel-Lindau's disease.

The pathogenesis of arterial aneurysms most likely starts with a congenital vestige of a more primitive embryonal vascular network, and most "berry" aneurysms are of this type. Trauma may produce an occasional case such as one seen by Bonnet where, after sphenoidal fracture, a saccular aneurysm appeared inside the sphenoid sinus, proven by arteriography, and leading to death by uncontrollable epistaxis. Although syphilitic and mycotic aneurysms are discussed, they are certainly infrequent at the present time. Probably the fusiform aneurysm of the internal carotid (as well as an occasional basilar aneurysm not mentioned) are primarily arteriosclerotic in origin.

The anatomico-clinical forms are discussed under the headings of internal carotid trunk, the circle of Willis, and the basilar trunk with the vertebral arteries.

Bonnet presents the detailed differential of internal carotid aneurysms in various parts of the cavernous sinus according to Jefferson's schema. In general, such lesions involve the ophthalmic trigeminal, with corneal anesthesia and orbital pain, together with oculomotor and abducens palsy, sympathetic signs

and exophthalmos based on venous stasis. In the posterior sinus, total trigeminal paralysis occurs, with total oculomotor palsy, abducens palsy, tearing from greater superficial petrosal compression, frequent exophthalmos and retinal signs of venous stasis. In the middle part of the cavernous sinus, the maxillary trigeminal is spared, total ophthalmoplegia ensues and moderate exophthalmos is found. In the anterior lesion (the infraclinoid carotid aneurysm of Dandy) the ophthalmic trigeminal alone is involved, with early and total oculomotor palsy and exophthalmos. A central scotoma is the usual sign of optic nerve involvement, and may lead to altitudinal defects, resulting finally in optic atrophy homolateral to the ophthalmoplegia.

(Such a detailed analysis by location is of interest, but in most cases the neurosurgeon would likely base his final localization on arteriography. The finding of exophthalmos, in particular, is certainly not as frequent as stated.)

Bonnet discusses at length the so-called fusiform aneurysm of the internal carotid on emergence from the cavernous sinus. Such an aneurysmal dilatation is probably atheromatous in origin and characteristically produces visual involvement. A homolateral central scotoma may be accompanied by other field signs of compression of the chiasm. In advanced cases optic atrophy may be accompanied by a temporal field loss in the opposite eye. Other mechanisms of optic nerve damage are thrombotic obliteration of the vasa vasorum and atheromatous extension into the ophthalmic artery (this latter is difficult to rationalize with the fact that even direct obliteration of the ophthalmic artery at surgery produces no visual defect—Ed.).

In discussing congenital berry aneurysms of the circle of Willis the author emphasizes that subarachnoid hemorrhage is frequently the first evidence of a lesion. Ophthalmoscopic signs of bleeding include retinal hemorrhages of nummular shape, more in the region of the papilla, and tending to be subhyaloid. Papilledema may follow, and may be accompanied by bilateral abducens palsy as a further sign of increased intracranial pressure. An associated third nerve palsy is of diagnostic importance—due to either a basal hematoma, direct aneurysmal compression, or tentorial herniation. He quotes the usual figure of 50 per cent mortality from the first subarachnoid hemorrhage. In detailing the various locations of aneurysms of the circle of Willis, the saccular lesion of the carotid trunk just prior to posterior communicating origin is characterized by frontal or retrobulbar pain and recurrent oculomotor palsy, both homolateral. When located on the posterior communicating branch the lesion produces similar signs. On the anterior cerebral or anterior communicating branches rupture may occur into the frontal lobes or ventricles and can produce serious motor and sensory signs. If the aneurysm is suprachiasmatic, chiasmal field defects and visual loss together with frontal pain may be the only signs. When the lesion occurs in the middle cerebral branch, rupture produces signs suggestive of hemispheric involvement, and if the oculomotor nerve is involved it is only by incisural herniation of the temporal lobe. Posterior cerebral aneurysms are infrequent and may involve the cerebral peduncle along with the emerging oculomotor nerve. In large lesions there may be hemiplegia with homonymous hemianopsia

due to direct rupture into the temporo-occipital region. Small aneurysms at the basilar bifurcation are usually silent until rupture occurs, but may produce bilateral third palsy. With rupture, cerebellar signs may occur. Bonnet discusses aneurysms of the interpeduncular space as a separate group, regardless of site of origin. They may produce diabetes insipidus, difficulty with heat regulation, arterial hypertension, difficulties with the sleep mechanism, adiposogenital dystrophy, gastro-intestinal hemorrhages, and other signs of hypothalamic disturbance.

Aneurysms of the basilar trunk and vertebral arteries are divided into two groups: (1) the large aneurysmal sac, and (2) the fusiform dilatation. The saccular lesions of the basilar trunk usually produce signs of a posterior fossa tumor, while the vertebral lesions cause a lateral displacement of the brain stem with resultant neurologic deficits. The fusiform dilatation of the basilar, probably arteriosclerotic in origin, may give trigeminal neuralgia, vestibular involvement, facial hemispasm, a cerebello-pointine angle syndrome, or signs of medullary compression.

Bonnet then reviews the clinical signs of diagnostic value. Spontaneous subarachnoid hemorrhage means an aneurysm in most cases, and if oculomotor palsy ensues, the diagnosis is almost certain. Agonizing pain in the eye, frontal region, or face is most important. He lists both ophthalmic and ophthalmoplegic migraine as suggestive, although Hamby tends to feel the incidence is not significant. (Only one case with a history of migraine was found in a study of 119 cases at the University of Michigan.) Ophthalmoplegia is a significant finding in many cases, and unilateral visual loss with optic atrophy, especially in association with ophthalmoplegia, is most suggestive. Any chiasmal syndrome should include aneurysm in the differential diagnosis.

In discussing the use of arteriography in diagnosis he points out that precise diagnosis can be made only in this way and that the findings are indispensable for operative treatment. Complications do occur, more frequently in arteriosclerotic patients, where hemiplegia may result.

The prognosis of patients with arterial aneurysms is serious. Fifty per cent will die from subarachnoid bleeding and in the majority surgery is indicated. Neurosurgical treatment can be either by carotid ligation in the neck, or by intracranial approach. Dandy's trapping operation, direct clipping, or muscle packing are utilized. Indications for treatment of aneurysms in the various locations are discussed. Lesions of the carotid trunk are best treated by ligation in the neck. Intact aneurysms of the circle of Willis require an intracranial approach, while ruptured lesions show a 50 per cent mortality after intracranial procedures —a figure inferior to the results of non-interference.

(Despite Bonnet's somewhat grim view of prognosis, it should be pointed out that those patients who present characteristic ocular signs usually have aneurysms which may be successfully treated. Prognosis for survival in a recent series studied at the University of Michigan was 80 per cent in subclinoid carotid, 68.5 per cent in supraclinoid carotid, 77.3 per cent in anterior cerebral, and 100 per cent in posterior communicating aneurysms. This further emphasizes the need

for careful consideration of the possibility of aneurysm by the ophthalmologist who often encounters the patient first.)

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Radiodiagnostic en Ophthalmologie. By EDWARD HARTMANN AND EVELYN GILLES. Masson et Cie., Paris, 412 pages, 497 illustrations, 5,000 francs (paper), 5,700 francs (cloth), 1955.

This opus on diagnostic ophthalmologic roentgenography is unique and fills a definite need as similar material has been accessible previously in widely scattered articles only. This fine work stems from the felicitous teamwork of Hartmann, an ophthalmologist interested in roentgenography, and Gilles, a roentgenologist specializing in the ophthalmic applications of Roengen rays. The volume stresses particularly the advances of the past twenty years, since Hartmann's previous book on the same subject, which was published in 1936, has for many years been both out of print and out of date. The presentation is essentially practical and designed to be equally useful to the ophthalmologist and to the roentgenologist. All the new techniques are discussed and illustrated including sectional radiography (of special value in the study of the optic canal and sphenoidal fissure), arteriography, phlebography and cisternography. The 17 chapters cover every phase of roentgenography that bears on ophthalmic practice. Adequately presented, as was to be anticipated, are the optic canal and sphenoidal fissure, sella turcica, orbital and brain tumors, lacrimal passages, intraocular foreign bodies, traumatic lesions, intracranial calcifications and congenital anomalies but unexpected enlightenment is also given on lesions of the teeth, cervical spine, petrosal pyramid, cranofacial skeleton and various miscellany. The numerous illustrations—averaging more than one per page—are the feature of this contribution. Among unusual pictures may be mentioned bilateral lenticular calcification, calcification of vitreous in phthisis bulbi, and sarcoidosis of the phalangeal bones. A companion volume on roentgen therapy in ophthalmology is much to be desired.

JAMES E. LEBENSOHN

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Current Review

OCULAR CHANGES IN DIABETES MELLITUS

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Diabetes mellitus is probably the most important and most common of the metabolic diseases. In discussing the visual prognosis of the diabetic, Cordes[1] has reviewed many of the features of this disorder. It may occur in the younger age group, including infants and children up to adolescent youth, and in the older adult age group, in which it occurs more frequently after the age of 40 and probably more frequently in women than in men.

Patients who suffer with diabetes present certain symptoms and characteristics which occur in nearly all. Although these may cover a wide range, it is usually found that these patients exhibit a hereditary tendency, racial susceptibility, obesity and some degree of emotional instability.

Anxiety and emotional stress are usually present in these patients[2]. Changes in the blood vessels are also common and arteriosclerosis has been present in older patients and in those who have had the disease for a number of years[3]. Capillary fragility has also been described[4]. Joslin[5] who has had the opportunity of contrasting the course of cases today with those of a generation ago, has noted the increased incidence of arteriosclerosis. He is, nevertheless, convinced that in his patients who have followed their treatment and who have been properly managed, there is a minimal amount of arteriosclerotic change. In cases of long duration, many older patients suffer with high blood pressure and a certain number are also known to develop Kimmelstiel-Wilson disease or intercapillary glomerulosclerosis[6]. These conditions will be discussed later.

OCULAR LESIONS

The occurrence of changes in the eyes of patients suffering with diabetes is often baffling to the ophthalmologist and in most instances finding a satisfactory explanation of their relationship to the disease itself is most challenging. It is often stated that ocular changes in young diabetics are much less common than among older patients. This is probably due to the fact that the younger patient has had the disease for a shorter period of time.

There does not appear to be any direct correlation between the use of insulin and the occurrence of ocular lesions in diabetes. It is generally agreed, however, that the proper treatment and control of the disease itself, with full cooperation from the patient, is important in limiting the extent of any ocular involvement.

The blood sugar concentration at any particular time usually bears no direct relationship to the occurrence of ocular lesions.

Changes in the refractive state. An exception to the above statement, however, may be the more or less sudden changes which sometimes occur in the refraction of the eyes in a patient with diabetes. Although there are differences of opinion as to how these refractive changes are produced, it is generally considered that the sugar concentration at any particular time may affect the refractive index of the lens of the eye. An increase in myopia or decrease of hyperopia of the eyes indicates an increase in the blood sugar, while an increase in hyperopia or a decrease in myopia signifies a decrease in blood sugar concentration. These changes in the refraction usually occur rather abruptly with a more or less marked and sudden change in the blood sugar of the patient. As a result, the patient would be conscious of a rather sudden change in the vision of his eyes. For the same reason, a gradual change in the blood sugar concentration of the patient over a longer period of time would also result in a gradual change in the refraction of the eyes.

Changes in accommodation. The accommodation of the eyes is often weakened, especially in younger diabetics who have had the disease for a few years and who are not under good control. In the opinion of the writer, the condition is not due as much to the effect of the sugar concentration on the ciliary body as it is to the inability of the lens of the eye to adjust itself in the act of accommodation as in the non-diabetic or normal individual. In younger presbyopes it might be necessary to prescribe a stronger lens than usual for near work at about 33 cm. This weakness in the accommodation of these patients may lessen with improvement in the general diabetic condition.

Ocular palsies. Paralyses of the extraocular muscles are not uncommon in diabetes, particularly in those of long duration and among the older patients, although the severity of the disease at the time of occurrence is not a factor. The sixth nerve is probably most frequently involved with limitation of external rotation resulting in the affected eye[7]. The third nerve and fourth nerve are probably next in order of frequency of involvement. The usual subjective symptom of this complication is sudden diplopia in moving the eyes in the direction of the involved muscle. In many of these patients, vascular hypertension and arteriosclerotic changes are also present. The prognosis for recovery of function is usually good and most of the cases recover. The specific cause for the occurrence of ocular palsies is not known. Kaplan[8] named hemorrhage or thrombosis, constriction of nerves by sclerotic vessels, cranial diabetic neuritis and intramedullary brain stem lesions.

Conjunctival capillary alterations. Ditzel *et al.*[9] studied the capillaries of the bulbar conjunctiva of 150 diabetics and 90 normal patients. They described an elongation of the venous capillaries, distention of the venules with aggregation of blood cells and a concomitant reduction of the blood flow. These findings may occur early in the disease. In the healthy children of diabetic mothers, they also described localized dilatations, constrictions, microaneurysms and sacculations, especially in the capillaries and venules of the bulbar conjunctiva. The vascular pattern was similar to that found in juvenile diabetes.

On the other hand, Cook[10], who studied the conjunctiva of a series of diabetic and non-diabetic subjects, found no specific conjunctival lesions in diabetes which were analogous to those which occur in the retina. Although his results failed to reveal any direct association between the conjunctival and retinal microaneurysms in the diabetic, there was an increased incidence of conjunctival lesions in the diabetic as compared with the control group. This increase was not significant, however, and was explained by the close relationship between conjunctival aneurysms and an associated hypertensive state.

Iris changes. Iritis in diabetics is perhaps no more common than in non-diabetics. Trauma to the eye or ocular surgery in a diabetic of long standing, however, may be followed by iritis which is more prolonged in its course and more severe than in others. The characteristic changes in the iris in diabetes are those found in the pigment epithelium. It has been known for some time that free pigment is liberated after swelling, edema and degeneration of the epithelium. In cases of long duration, atrophy of the iris occurs.

Very occasionally, a non-inflammatory condition known as rubeo-irides or diabetic rubeosis may be observed in cases of longer duration. It is characterized by the proliferation of newly formed blood vessels around the pupillary margins on the anterior surface of the iris. It can be seen as a dark red ring on direct examination, or by examination with the slit lamp. Other ocular complications, especially retinopathy, are also present in these cases and they are often complicated by secondary glaucoma. When surgery is performed on these cases for glaucoma or for any other reason, the results are often unsatisfactory because of the occurrence of hemorrhage, secondary iritis, and a prolonged recovery.

Lens changes. Cataract has always been considered rather common in diabetes. Most patients, however, who suffer with diabetes are in the age groups in which the ordinary senile type of cataract occurs. There has never been any difference found between the biochemical changes that occur in the crystalline lens with the development of the cataract in diabetes and those found in the ordinary senile cataract of a non-diabetic. Differences in the appearance, however, of what has been called a diabetic cataract have been described and attempts have been made to explain the etiology of cataract of diabetics. O'Brien[11] felt that the lens was subjected to a higher concentration of sugar in the surrounding fluids in diabetes than in the normal and this condition could result in opacification of the lens when it continued over a period of years. The blood sugar concentration at any particular time, however, has no relationship to the development of cataract. On the other hand, the duration of the disease in any case does appear to be related to the development of the cataract. O'Brien, Molsberry and Allen[12] described the diabetic cataract as occurring in younger patients as well as children and it presented a rather characteristic appearance. It differed from the ordinary form of cataract principally because of its subcapsular involvement, rather rapid development, and involvement of both eyes. It presents a rather characteristic appearance with a large number of whitish, flake-like opacities scattered over a wide formation of subcapsular vacuoles. It continues to increase and reach a stage of complete opacification. Kirby[13] also found this condition to occur particularly in

the very young and those diabetics up to the age of 25 years. In a later study of 260 young diabetics under the age of 21 years, O'Brien and Allen[14] found this type of cataract formation to occur in 14 per cent.

In the patient with diabetes, surgery for removal of the cataract can be performed when indicated. The disease itself is not a contraindication (see Treatment).

Retinopathy. Retinopathy is perhaps the most dramatic and pronounced manifestation of diabetes in the eye. This was formerly described as a "retinitis" and also a "retinosis," but the term "retinopathy" is more descriptive and all-inclusive since it emphasizes the degenerative nature of the changes occurring in retinal vessels and in the retina itself.

The characteristic diabetic lesions which can be observed in the retina itself consist chiefly of small, round hemorrhages and yellowish, glistening spots which have been designated by many as exudates or patches. In a typical case, the small round hemorrhages are discrete and can usually be observed with the ophthalmoscope. They are located in the deeper layers of the retina. The yellowish glistening patches may also appear to be small and more or less round. They are usually found in rather close association with the hemorrhages, but, with progression of the disease, they show a tendency to arrange themselves around the macular region and in most instances encircle it. In an early stage, only one or two lesions may be present in the retina but additional lesions will appear as the disease progresses. In long standing cases, the glistening patches seem to lose their early lustre and take on a dirty-yellow or waxy appearance. They might be described as hard patches with rather well demarcated edges in contrast to the white "cotton-wool" exudates with fluffy margins commonly seen in the retinopathy of hypertension and nephritis. With progression of the disease, the hemorrhages may also become larger and in very late cases, extensive preretinal and even vitreous hemorrhages may occur. The occurrence of these lesions in the retina does not depend on the severity of the diabetes but rather on the duration of the disease. The retinopathy still defies satisfactory explanation, as is discussed later, but it might be explained, in general, as a local circulatory disturbance in the retina which results in an impairment of nutrition which is followed by appearance of the lesions. The actual process was explained by Elwyn[15] as a peristasis or "prestasis" which occurs in the terminal vessels. The terminal vessels then become dilated which is followed by hemorrhages from diapedesis. As the dilatation persists, the nutrition becomes chronically deficient with a diminished supply of oxygen and secondary changes, such as fat and lipoid deposits, occurring. Pathologic changes in the retina of young diabetics were found by O'Brien and Allen[14] to occur in 23 out of 555 patients under 31 years of age. The lesions observed were similar to the hemorrhages and patches found in older patients.

Ophthalmologic examination of 1300 diabetic patients by Dollfus[16] revealed that 569 or 43.7 per cent had retinopathy. The duration of the diabetes appeared to be the main factor in the occurrence of the retinopathy. He found retinal lesions to be present in 25 per cent of the cases which were less than seven years in duration. In those with a duration over fifteen years, 75 per cent to 88 per cent of the diabetic patients had retinal lesions.

In recent years, the study of flat preparations of the entire retina has greatly advanced our knowledge of the vascular process associated with the occurrence of the retinopathy. By employing new methods of staining, it was possible to examine the entire vascular system of the retina and thereby to present a clearer and more detailed description of the changes. In 1944, Ballantyne and Lowenstein[17] described the punctate retinal hemorrhages in diabetes as small aneurysmal sacs which were lined with endothelium and connected with the capillaries. This was later confirmed by Friedenwald[18] and also Ashton[19]. Friedenwald demonstrated large numbers of these capillary aneurysms in flat specimens of the retina. They were found most frequently in the central region but occasionally in the far periphery. Microaneurysms occurred principally on the venous side of the capillary bed. These capillary aneurysms may occur rarely in the non-diabetic but, according to Friedenwald, they are different in size, number and appearance. They are so numerous, however, in diabetic retinopathy with the surrounding hemorrhages and exudates, that they represent a characteristic picture of the condition. In diabetes, the aneurysms represent a primary vascular lesion in the retina, while in other diseases they occur in response to local injury. A cluster of exudates could sometimes be found to surround the aneurysm, and hemorrhages were also seen adjacent to them. The exudates occurred in the outer fibrillar layer while the aneurysms were located in the inner nuclear layer. Many of the aneurysms have thin walls but in others they were thickened and hyalinized. Sometimes the thickening of the walls almost obliterates the lumen. Friedenwald also felt that the exudates were formed by a leakage of plasma through the wall of the aneurysm. Many of these microaneurysms are too small to be observed with the ophthalmoscope. Therefore, in early or mild cases, the lesion would escape diagnosis. But when they are persistently present for some time, they can be observed as small, punctate petechia.

The arterioles of the retina were also studied post-mortem by Ashton[20] who injected them with india ink and stained the flat preparation by the periodic-acid Schiff method. Ashton found that the retinal arterioles also are subject to a type of hyaline degeneration as severe as that in other parts of the vascular system in diabetes. Hyalinization of the terminal arterioles and precapillary vessels of the retina leads to a narrowing and gradual occlusion of the lumina resulting in atrophy of the arterial side of the capillary bed and the formation of new channels on the venous side of the capillary bed. Microaneurysms also occur from the capillary loops. This severe arteriolar involvement should be regarded as a late development of the diabetic process itself and not as an added hypertensive complication, since it did not occur in non-diabetics with only hypertension or arteriosclerosis.

In 1936, Kimmelstiel and Wilson[6] described lesions in the glomeruli of the kidneys known as intercapillary glomerulosclerosis. These lesions consisted of microaneurysms very much like those found in the retina in diabetes and also hyaline nodules in the glomeruli of the kidneys. Kimmelstiel-Wilson disease, as it has come to be known, is found in diabetics with retinopathy. The patients are usually 50 years of age or more and have had diabetes for a number of years.

Retinopathy is an essential factor. In addition, the patients have vascular hypertension, edema and albuminuria. The specific diagnosis, however, can only be made at post-mortem after pathologic examination of the kidneys. Sodeman[21] divides glomerulosclerosis into (a) diabetic and (b) hypertensive glomerulosclerosis. In diabetes with intercapillary glomerulosclerosis, the pattern of renal function and mechanisms is similar to that of glomerulonephritis, but it is definitely an entity separate from this condition and hypertensive glomerulosclerosis as well.

Dana and Zubrod[22] found Kimmelstiel-Wilson lesions in diabetic patients ranging in age from 15 years to over 60 years. Most of the patients were between 30 and 60 years old. The diabetes mellitus apparently exists for some years before the kidney nodules develop. According to these authors, about 78 per cent of the diabetic patients with Kimmelstiel-Wilson nodules in the kidneys have capillary aneurysms of the retina. On ophthalmoscopic examination the aneurysms usually appear as multiple, deep, punctate hemorrhages. Both Friedenwald and Ashton felt that Kimmelstiel-Wilson glomerulosclerosis and retinal aneurysms are manifestations of the same vascular process. The retinal disease in diabetes precedes the renal lesion, since at least five of the cases examined by Ashton showed a retinopathy without any glomerular involvement, while the more severe forms were associated with glomerulosclerosis. It has been my own feeling that Kimmelstiel-Wilson disease occurs at a later stage in the course of diabetes and that a presumptive clinical diagnosis can be made on the basis of the symptoms enumerated.

Taylor[23] who examined the fundi of 110 diabetics discussed the relationship of the retinal and glomerular lesions in this disease. The retinal changes always appeared earlier than the renal and the duration of the diabetes was the most important factor in the development of retinal and renal lesions. This is explained, of course, by the fact that since the use of insulin has greatly prolonged the life of the diabetic, the incidence of retinal and renal lesions is much higher in these patients today than in former years.

Vascular hypertension may also be present in diabetes without evidences of renal impairment. Other patients may present evidence of both conditions. According to Lundbalk[24], arterial hypertension is very common. It was present in 52 per cent of males and 84 per cent of the females. The changes of hypertension which might be observed in the retina are additional hemorrhages which are streaked and more superficially located than those characteristic of the diabetic condition. Later in the course of the hypertensive disease, the presence of edema in the neighborhood of the disc and macula may modify the ophthalmoscopic picture.

Increased capillary fragility is an abnormality occurring in the course of diabetes which has received much attention. According to Rodriguez and Root[4], it was found in 40 per cent of 100 unselected patients. It was present in nearly all cases with retinopathy whether or not hypertension was present. In 82 of their patients with diabetic retinitis, 41.4 per cent were under 40 years of age. Capillary fragility was found as early as 21 years of age but only in cases of long dura-

tion. They also found that the use of rutin improved the capillary fragility to normal, but it had no effect on the retinopathy. Dicoumarol and rutin were employed in these cases by MacLean and Brambel[25].

Experimental and clinical studies. In recent years, lesions very similar to the Kimmelstiel-Wilson nodules were produced in rabbits by the intramuscular injection of 75 mg. of cortisone daily for two weeks[26]. These typical lesions have also been found in the kidney of a non-diabetic who had long and intensive treatment with corticotropin (ACTH). These observations led Becker[27] to study the role of ACTH and adrenal-cortical function in diabetes with and without retinopathy. Flat preparations of whole retinas permitted a clearer differentiation of diabetic retinopathy from the fundus changes found in hypertension, atherosclerosis and renal disease. Diabetic retinas, stained with periodic acid-fuchsin, showed discrete, saccular aneurysms in the capillaries. These occasionally had thin walls but were frequently enclosed in thickened, laminated layers of hyaline material. Exudates which were caused principally by leakage of protein and accompanied by hemorrhages surrounded the aneurysms. Newly formed capillaries were found in the more advanced stages. These characteristic aneurysms associated with hyalinized nodules are also found in the kidneys with intercapillary glomerulosclerosis. Attempts were made to produce diabetic retinopathy in rabbits which were made diabetic with alloxan. ACTH was administered, since this hormone had been observed to increase capillary aneurysm formation in the retina. The ophthalmoscopic picture of an early diabetic retinitis developed. Flat preparations of the retina of some of the rabbits revealed lesions similar to those found in the kidneys. In the rabbits which were given cortisone alone, however, the kidneys revealed Kimmelstiel-Wilson-like lesions but there were none found in the retina.

It was felt that both the pancreatic lesions and an excessive amount of ACTH in a diabetic are factors in the development of both diabetic retinopathy and intercapillary glomerulosclerosis. It is known that increased ACTH secretion occurs in pregnancy, infections and in poor diabetic control during which retinopathy is aggravated.

Becker weighed the adrenals of 155 diabetics at autopsy and found correlation between the presence of lipoid-laden vacuolated cells in the zona fasiculata of the adrenal cortex and the presence of Kimmelstiel-Wilson lesions in the kidneys. In diabetics without the kidney lesions, there was a decrease in the incidence of lipoid vacuolation in the cortex. The prolonged administration of ACTH was associated with increased lipoid secretion in the zona fasiculata. It appears that lipoid vacuoles in the diabetic without kidney lesions may be interpreted as a compensatory decrease in adrenal cortical activity and that normal or relatively excessive capacity in the diabetic may be related to the development of both the kidney and retinal lesions.

In diabetics with retinopathy, the adrenal cortex is apparently responsive to exogenous ACTH, as indicated by the eosinophil depletion, whereas the adrenal cortex of diabetics without retinopathy responds much less or not at all. Bilateral adrenalectomy might, therefore, cure diabetic retinopathy. In 1953, Bookman

et al.[28] presented a study of five cases of diabetes which developed in patients receiving steroid treatment. They described this as a type of steroid diabetes which could develop in humans who were being treated with ACTH or cortisone. None of the patients they reported on had glycosuria or hyperglycemia before the therapy was started. The evidences of diabetes disappeared when the therapy with ACTH was reduced or discontinued. The glycosuria was increased when the dosage was increased and reduced when the dosage was decreased.

According to McCullagh and Alivisatos[29], Cushing's syndrome may be relieved by x-ray therapy when caused by excessive corticotropin from a pituitary tumor, whereas in cases due to adrenal hyperplasia, removal of about 80 per cent of adrenal tissue provides complete control.

Iannaccone and Kornerup[30] found an elevation of the total plasma lipids which they considered significant in patients with diabetic retinopathy. On the basis of Becker and Friedenwald's work, they suggested that this increased lipid content might be related to increased cortical activity.

Goodman[31] also felt that the retinopathy in diabetics results from a metabolic disorder characterized by a hormonal imbalance.

Based on the work of Chow[32], Becker *et al.*[33] studied the clinical and laboratory evidence regarding excessive adrenal cortical function and vitamin B_{12} deficiency in pathogenesis of diabetic retinopathy. The intramuscular injection of 50 gamma of vitamin B_{12} given to 22 diabetics with retinopathy produced an 8-hour excretion of vitamin that averaged 19 gamma. Thirteen diabetics without retinopathy excreted an average of only 4.2 gamma. The average excretion of vitamin B_{12} in non-diabetics was found to be 9.6 gamma. They felt that these findings were consistent with the thesis of an increased adrenal cortical activity associated with diabetic retinopathy. The high levels of adrenal cortical hormones could prevent the retention of vitamin B_{12} in these cases. Moreover, since vitamin B_{12} has been found to be beneficial in the treatment of diabetic neuropathy, it could be taken as additional evidence for assuming that diabetics with retinopathy are more depleted of vitamin B_{12} than diabetics without retinopathy.

The role of glutathione in the production of diabetes has received the attention of Lazarow[34], Griffith[35] and Conn *et al.*[36] The administration of ACTH is accompanied by a decrease in the concentration of glutathione in the blood as well as an increase of uric acid content in urine. It was considered that some product of purine metabolism might have an effect similar to alloxan in reducing the glutathione which is necessary for normal action of the enzyme system and would thus impair the function of the pancreatic B-cells. Conn and associates[36] made studies on a normal young man and found that intravenous administration of large amounts of glutathione reversed the hyperglycemia and glycosuria produced by the administration of ACTH. If, therefore, a retinopathy occurs in the presence of excessive adrenal cortical secretion in diabetics, it is also plausible to assume a relationship between the latter and a reduction of blood glutathione in these patients.

In the last few years the alpha cells of the islets of Langerhans have received attention. There is evidence to show that the alpha cells are responsible for a

hormone-like substance called glucagon which is a hyperglycemic factor and antagonistic in action to insulin. Its production is stimulated by a growth hormone of the anterior pituitary. This adds something to the known relationship between the pituitary and diabetes. Alloxan, which destroys the beta cells, does not destroy the alpha cells and therefore does not affect the secretion of glucagon. McQuarrie *et al.*[37] reported studies on a small series of infants suffering from spontaneous hypoglycemosis in whom almost complete absence of pancreatic alpha cells appeared to be the most likely etiological factor. The administration of adrenocorticotropic hormone was found to be highly effective in control of the hypoglycemia. Whether or not an excess of glucagon in diabetic patients might have some effect in the production of retinopathy is at the present time only speculative but merits future investigation. It should be possible to create a diabetic state by stimulating its production as well as by suppressing insulin, while on the other hand, suppressing its production should relieve such a condition. This might also explain the development of retinopathy in a patient with a relatively normal or even low blood sugar concentration.

Alivisatos and McCullagh[38] used glucagon to test patients with insulin sensitivity and to study hepatic glycogen reserves in the regulatory mechanisms during hypoglycemia. They administered 0.6 mg. of glucagon intravenously in 50 cc. of isotonic sodium chloride solution to normal patients and others with various metabolic diseases who were known to be insulin-sensitive. From their studies of this small group of patients they felt that the application of the glucagon tolerance test appeared to be safe and practical under standard conditions, and that it could be valuable for detecting insulin sensitivity in patients with hypoglycemia unresponsiveness, especially when an insulin tolerance test would be dangerous.

Hypotony. Ocular hypotony in diabetes has received casual attention in the past as a factor in the occurrence of diabetic retinopathy. Recently, however, Weinstein[39] was convinced that, since hemorrhages in the eyegrounds almost never occur in cases with increased intraocular pressure (glaucoma), hypotony must be an important factor in the occurrence of retinal hemorrhages in diabetes. He found that in 19 of 20 cases of diabetic retinopathy, the ocular tension was less than 20 mm. of mercury. He also referred to Ortiz who obtained similar results. He is of the opinion that "hemorrhagic diabetic retinitis develops in cases which combine low intraocular tension and increased petechial disposition."

Vitreous involvement. Hemorrhages into the vitreous may occur in advanced cases with a marked hemorrhagic tendency. The vision of the patient may become so greatly impaired because of extensive hemorrhage into the vitreous that even light perception is lost. On examination the pupil in the affected eye will be black and no fundus reflex can be obtained. This is often referred to as the 8-ball pupil. In some cases newly formed blood vessels are found with proliferating bands of tissue extending forward from the retina into the vitreous. Further serious complications in such cases are secondary glaucoma and secondary detachment of the retina. There is a slight possibility that small hemorrhages in the vitreous might clear to some degree with a corresponding degree of visual improvement. They have a tendency to recur, however, and eventually lead to total loss of

vision. Treatment of this condition is not satisfactory. Cordes[1] followed the procedure of Guyton and Reese in employing roentgen therapy in one case which received 6000 r. The vision improved sufficiently for the patient to go about comfortably but the retinopathy gradually progressed and resulted in a more extensive retinitis proliferans.

Optic nerve involvement. Very occasionally, an optic neuritis may occur in a patient with diabetes but these cases are rare. This is probably also true of retrobulbar neuritis. According to Walsh[40], this diagnosis in a diabetic is subject to question. He does, however, mention a hole in the macula as a more common occurrence and one that may often escape recognition. In the average case, however, the optic nerve is scarcely ever involved[41]. The margins of the optic nerve head are usually well outlined and the color normal. In very late cases the disc may appear to be waxy pale in color. When optic atrophy does occur in the later stages of diabetes, it is probably due to the generalized arteriosclerotic changes. As a result of these changes in which the retinal vessels are involved, the nutrition of the retina and optic nerve is impaired over a period of years with resulting degenerative changes and optic atrophy.

Lipemia retinalis. Lipemia is, today, a comparatively rare occurrence among diabetics. This is probably because of the regular use of insulin and improved management of the disease. It is characterized by an ophthalmoscopic appearance of a creamy pink to a chocolate color in the retinal vessels associated with an increase in the fat content of the blood. The vessels appear somewhat wider than normal and usually take on a creamy color when the fat content rises to about five to eight per cent. The condition usually occurs in the younger diabetics, although it has been observed in older patients. Cases of lipemia have also been reported in non-diabetics. In the past, the condition was often found in comatose patients, but, with the regular use of insulin, its occurrence is much less frequent. When it does appear, the prompt use of insulin is followed by improvement.

Juvenile diabetes. Ocular lesions in younger patients with diabetes are not as varied and pronounced as in most of the older patients. In a series of 260 patients under 21 years of age, O'Brien and Allen[14] found changes in the lens in 36. In most of these patients, the diabetic condition had been uncontrolled. With proper treatment and control, the opacities failed to progress after a period of six months.

Perhaps the most frequent manifestation of diabetes in these patients is retinopathy. O'Brien and Allen found changes in the retina due to diabetes in 23 out of a group of 555 cases under 31 years of age. Most of the lesions observed were similar to those which occur in older patients. I have recently observed retinopathy in a young man, 26 years of age, who had diabetes since the age of nine years. He had a marked bilateral retinopathy, many petechia and larger hemorrhages as well as numerous glistenig patches in the retina. The vision was markedly reduced in both eyes. Advanced cases such as this, however, are not common in the younger patients, especially if the diabetes has received proper and regular treatment.

In a series of 40 diabetic children, Guild *et al.*[42] found that the retinal lesions

may be seen relatively early in the course of the disease. The incidence of these complications increases with the length of duration although good control of the disease was found to modify the severity and progression of the lesions.

Changes in pregnancy. Diabetic women who have had the disease for a comparatively short period of time may show no signs of retinopathy or other ocular involvement and may go through a pregnancy uneventfully. Diabetics, however, are known to be more susceptible to complications during the course of a pregnancy than non-diabetic women. The offspring of diabetic mothers are also more prone to develop diabetes and to suffer with other congenital manifestations. It seems that a normal uncomplicated pregnancy in a diabetic is related to the extent of the ocular involvement, particularly retinopathy and the severity of retinal hemorrhages already present. According to Beethem[43] the presence of a retinopathy in a diabetic mother offers a poor prognosis for normal delivery and vision.

Treatment of ocular changes. The diabetic patient should be treated by the endocrinologist or internist, who should receive reports from the ophthalmologist regarding the patient's ocular condition after each examination.

The question of whether or not ordinary cataract is more common in the diabetics than in non-diabetics has been disputed, but most authorities agree it is more common in the diabetic. In my own experience, cataract does occur more frequently in diabetics than in others belonging to the same age group. Since most of the older diabetics with cataract are in the same age group with non-diabetics who have ordinary senile cataract, the former can be operated on for removal of the cataract just as in the latter group. It is important that the diabetes be under control at the time of operation. The desirable level of the blood sugar at the time of operation is that which is best for the general condition of the individual patient as determined by the physician who has been managing the patient. It is important in these cases to determine also, if possible, the presence of a retinopathy. With satisfactory control of the diabetes and with the absence of retinopathy, the likelihood of a satisfactory result in such an eye is practically as good as in a non-diabetic. It should be remembered, however, that the vessels of the iris in diabetics are more susceptible to hemorrhage and the possibility of hemorrhage is greater both during the operation and post-operatively. Furthermore, the presence of a retinopathy increases the danger of post-operative hemorrhage and delayed healing with a final disappointing result.

In a series of diabetic patients who had cataract surgery, Townes and Casey[44] found 49.2 per cent to have operative or post-operative complications. These included nearly all of those usually encountered, with hyphemia occurring in 22 per cent of the diabetics as compared with 10 per cent in non-diabetics. They concluded, however, that with careful pre-operative preparation there should be no hesitation in performing cataract surgery on diabetic patients.

As previously stated, most of the true diabetic cataracts occur in the younger patients. Since the lenses in these cases are still soft, removal of the cataract should be accomplished by linear extraction. In the average case, the possibility for obtaining a satisfactory result is good.

In considering the therapy of the ocular complications of diabetes, two important features of the disease should again be mentioned. Many patients with the disease are subject to emotional stress and strain. Hinkle and Wolf[2] studied more than 50 patients for the effects of mental and emotional strain which they found might be an important factor in the onset and course of the disease. In my own experience also, an emotional factor has been found to be present in most of these patients. When present over a period of years, this could prove to bear a relationship to dysfunction of the autonomic nervous system as well as the endocrine system.

Another important feature in the treatment of the ocular complications is the need for proper management and rigid control of the diabetes itself. This has been emphasized by a number of authors, particularly with regard to the occurrence and progress of the vascular and retinal lesions. Joslin *et al.*[5] have shown that their patients who received the proper treatment and management and who remained under rigid control showed a minimum of vascular lesions particularly in the retina, after having the disease for more than 25 years.

In support of this premise, Wilson *et al.*[45] presented an extensive study of 247 younger patients who had the disease for a minimum of 10 years and a maximum of 34 years. According to these authors, "ideal or perfect control implies that a diet planned to provide proper amounts of minerals, vitamins and calories, derived from a proper proportion of carbohydrate, protein and fat, has been so well utilized by means of an adequate insulin effect that blood and urine tests are invariably normal." With excellent or good control in this series of patients they reported that none showed advanced calcification or retinopathy even after 20 to 34 years of diabetes and no case of diabetic nephropathy developed. Diabetic nephropathy did occur in 62 patients with poor or fair control. In 89 of these patients, or one-third of the number, no retinal hemorrhage or retinitis was found. Thirty-five of these patients had the disease for more than 20 years. In 103 cases, of 20 to 34 years' duration, 3 of the 4 with excellent control showed no retinal lesions. Of 54 cases with moderate to marked retinopathy, none had excellent control and all but 5 had fair or poor control. Fifty-five among 80 cases who lived for at least 20 years under poor or fair control showed severe, degenerative lesions, i.e., calcified arteries, retinitis, or nephropathy. It was emphasized that control of the diabetes is thus more important than any known factor such as duration or severity in preventing these degenerative lesions.

The importance of proper diet and "total caloric regulation" was also emphasized by Sherrill[46] and others. Guild *et al.*[42] also stated that patients consistently well controlled could remain free of vascular lesions for as long as 18 years and might show only a minimum of lesions as long as 22 years after onset.

On the other hand, Tolstoi[47] advocated a "free diet for diabetics," without influencing the occurrence of vascular lesions. He was supported in this view by Dolger[3] who felt that all diabetics would develop vascular damage and retinopathy after a duration of 25 years, regardless of the degree of control or the use of insulin. Larsson *et al.*[48] also stated that the duration of the diabetes influences the occurrence of retinopathy, arteriosclerosis and albuminuria, regardless of the

diet, and that a "free diet" is preferable in these cases. They felt that measured diets in children provided no more protection against degenerative vascular lesions than free diets with adequate insulin therapy.

In order to evaluate the state of the diabetic process, Mohnike *et al.*[49] advocated a determination of protein bound sugar, as an indicator. They found that protein bound sugars are low in well controlled, complication-free patients. But the level rises in cases with retinopathy, nephropathy and arteriosclerosis, even when proper treatment keeps blood sugar within reasonable limits.

In the absence of any more specific therapy for the vascular complications and retinopathy in diabetes, multivitamins, vitamin B_{12}, methiscol, C.V.P. (with ascorbic acid), hesperidin and rutin have all been employed in order to retain the integrity of the vessels and normal capillary fragility. It is possible that any of these may benefit some early cases and can be administered as a routine measure. Their specific effect is difficult to evaluate except after use for long periods of time, and reliable reports of any beneficial effects are still lacking.

Rodriguez and Root[4] found that the use of rutin in adequate dosage restored capillary fragility to normal, but that it had no effect on the retinopathy. MacLean and Brambel[25] also employed rutin to decrease the capillary fragility and also administered rutin with dicoumarol for the treatment of retinal and vitreous hemorrhages. Levitt *et al.*[50] prescribed 100 mg. of ascorbic acid three times daily for one month. This was followed by 20 mg. of rutin three times daily for two months, and then 40 mg. daily for another month. They did not claim that any specific improvement was obtained.

Saskin *et al.*[51] reported the use of testosterone in the treatment of 28 cases of diabetic retinopathy. This was administered intramuscularly, in doses of 50 mg. the first week, followed by 25 mg. the second week and then alternating the 50- and 25-mg. doses for a course of at least eight injections. They reported satisfactory results in their cases, but their results have not as yet been confirmed by other workers.

Bedrossian and his co-workers[52] treated 77 men and women between the ages of 45 to 65 who suffered with diabetic retinopathy. Testosterone propionate 50 mg. alone or combined with estradiol benzoate was given to 51 patients intramuscularly at weekly intervals for five months. Saline was administered as a control to 26. According to their criteria none of the patients showed any improvement. Many in both groups noted subjective improvement in vision and well being, but no such improvement was found objectively.

Attempts at direct treatment of the diabetic retinopathy have thus far been without satisfactory results. The therapeutic measures which have been mentioned may have a tendency to reduce the extent of the vascular and retinal pathology. They cannot be called specific in any sense, and the results are not as yet generally agreed upon. Sufficient knowledge is still lacking with regard to the etiologic factors and pathologic processes responsible for the vascular changes and ocular lesions occurring during the course of the disease. Other related disorders which are still poorly understood or not even recognized must in the future receive further study. This may provide the additional knowledge

necessary to explain the presence of the retinopathy more exactly and also to provide a more specific and satisfactory form of therapy.

Visual prognosis. The loss of vision which results from the ocular involvement in diabetes is severe and widespread. Most physicians will probably agree with Cordes[1] in his conclusion, regarding the visual prognosis, that the patient requires the best possible control of the diabetes and that full use should be made of all available knowledge regarding the condition.

The prognosis for improvement of the vision by surgery in diabetic patients with cataracts is generally good. It is important that the diabetes be well controlled before the time of operation and that no retinopathy be present. The latter may lead to post-operative complications and a poor result.

The prognosis for vision in diabetics with retinopathy is still not good. In the experience of most writers, the incidence of retinopathy increases with the duration of the disease, especially in the average case, and a patient who has had the disease for 20 to 25 years will be almost certain to have a retinopathy. With progression of the retinopathy, the vision usually becomes progressively worse.

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Clinical Practice

ACCOMMODATION AND REFRACTION

ON THE SUBJECT OF THE PRESCRIPTION OF PRISMS AND ESPECIALLY THOSE WITH AN OBLIQUE AXIS

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Practitioners often hesitate to prescribe prisms, especially when it is a question of simultaneously correcting both a vertical and a horizontal deviation for which oblique axis prisms are required. Unlike horizontal deviations of the ocular axes, a small vertical deviation will often result in subjective disturbances. When it is remembered that the amplitude of vertical fusion is from 3 to 6 degrees, it is easy to see that patients with a vertical deviation of 1 or 1½ degrees may complain, not of diplopia, but of indistinct vision. This is a more frequent occurrence than one might think, especially in the older age groups. Prismatic correction usually causes the subjective disturbances to disappear. For vertical deviation, it is generally appropriate to correct about three-fourths of the latent deviation. Inasmuch as a vertical deviation is frequently accompanied by horizontal phoria, it is often necessary to correct both deviations simultaneously.

Theoretically, a prism with a vertical effect might be used on one side and a prism with a horizontal effect on the other; in practice, however, it is better to prescribe a prism with an oblique base for both eyes. Although the calculations needed to determine the effect of prisms with an oblique axis are not complicated, the practitioner can scarcely be expected to make them every time he has to prescribe oblique axis prisms. The tables that have been constructed to give the value of a prism with an oblique base are useful, but they are not easy to read and there is always the possibility that a mistake may be made in regard to the direction of the base of the prism. With Allen's chart, however, which is unfortunately not widely known, it is very easy to get the strength and the base of an oblique prism immediately. By reference to the chart, it can be seen that both vertical and horizontal deviations can be simultaneously corrected by using a prism with an oblique base that is only slightly stronger than the one needed for correction of the vertical deviation alone.

Among the conditions for which prisms are especially indicated are latent strabismus, acute concomitant strabismus, paralytic strabismus, and insufficiency of divergence, which is not so rare as it is sometimes thought to be.

Finally, Allen's chart can also be used in cases in which it is desirable to obtain a prismatic effect by the oblique decentration of corrective lenses.

Comment: This condensation presents a summary of the clinical recommendations which are incorporated in the original paper, which, itself, consists mostly of a review of the general subject of prisms including their theory, method of calibration, relation to the lens diopter, and procedure in combining two prisms with their base-apex lines at right angles.

To facilitate the latter operation, the author suggests the use of the Allen Chart (Arch. Ophth. (1939, *22:* 113) which indeed does permit approximation of the amount and axis of one oblique prism substituted for a combination of two with base-apex lines at right angles. Most ophthalmologists, however, have sufficient knowledge of the physical principle of the resolution of forces and the Pythagorean theorem, so that with the aid of a trigonometric table of natural functions of angles the power and position of the base of the substituted prism can be determined easily if the Allen Chart is not available.

Prismatic effects in the decentration of both spherical and cylindrical lenses must also be considered in final refractive corrections, and present little difficulty if the axes of the latter are horizontal and vertical. Oblique axes complicate the matter, and the author considers the question of these beyond the scope of his paper. Actually, the dioptric power of an oblique cylindrical or sphero-cylindrical lens in the horizontal or vertical meridian can easily be determined by again using the trigonometric tables and multiplying the power of the cylindrical component by the $\sin^2$ of the angle of the axis to the horizontal.

Judging from the occasional reports in foreign journals, ophthalmologists in European and Asiatic countries prescribe base in and base out prisms to a much greater extent than do those on this continent. Experience over many decades has convinced most of the latter group that prisms base in or base out are rarely indicated in lateral heterophorias as, for the most part, they seem rarely to produce comfortable single binocular vision. As for paralytic strabismus, few American ophthalmologists would attempt any correction by prisms realizing that in such cases there can be no constant angle of deviation of the two visual axes for different fixations such as is present in comitant heterotropia. Even in the latter condition, prisms base in or base out can rarely be used with any hope of comfort, and usually seem to make matters worse.

Among the very few indications for such prisms which this commentator has found in his experience are deficiencies in fusional convergence for near fixation, in which prisms base in for near are very occasionally helpful, and in the comitant esotropia which occasionally follows an abducens paralysis from which the patient has otherwise recovered. If such a patient, usually elderly, has had good lifelong single binocular vision, the diplopia which ensues is quite annoying and, in many cases, a prism which puts the usually small deviation into the extra-macular fusion fields, will permit fusion with comfort. These cases are apparently included in those considered by the author as presenting an insufficiency of divergence.

Vertical heterophoria, or heterotropia of small amount, however, is a different story and Dr. Franceschetti seems much more enthusiastic about its relief with vertical prisms. Provided the condition is comitant and small in amount, not more than 4^{Δ} or 5^{Δ}, vertical prisms are the treatment of choice in such cases and sufficient prism power to place the images safely within the extra-macular fusion area will nearly always insure comfort. The amount of prism power to be used, according to the author, is generally about ¾ of the actual deviation, but this rule seems to ignore the actual fusional vergence amplitudes in the vertical directions, which can easily be determined in all cases with single binocular vision.

The amplitudes of fusional vergence in both horizontal and vertical directions are, of course, not absolute values, but are dependent upon the method by which they are measured, and any ophthalmologist who uses any acceptable method must decide how much of the amplitude found can be used comfortably in any given direction to compensate for the heterophoria present. Only in this manner is it possible to arrive at prism corrections which will be efficient and comfortable.

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THE DUOCHROME-STAR TEST

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The chromatic aberration of the eye can be used to refine the subjective examination of refraction by employing light of various wave lengths as a "carrier" for picturing black objects on the retina. The duochrome-star test which has been devised on this principle is a modification of Clifford Brown's red-green test. It consists of a six-pointed asterisk or clock dial chart which is symmetrically built up from black double-lines (strips), each 2 mm. wide and 1.5 mm. apart and intercrossing at the center. This asterisk is placed over an equally transilluminated circular ground-glass, one half of which is covered with red foil, and the other half with green foil. The main black double-lines of the asterisk are vertical to the red-green border line, the secondary double-lines are arranged at 60 degree angles to both sides of the main double-lines. At the periphery of the circular ground-glass short lines are arranged at intervals of 5 degrees. The test ground glass rotates and an illuminated scale gives the angle at which the axis of the cylinder should be set.

The duochrome-star test improves the Clifford Brown test in two ways. The setting of small cylinders is refined by the arrangement of the double-lines: parallel lines alone are insufficient for the determination of the axis of a mild astigmatism. It is possible to correct simultaneously, using a spherical and cylindrical lens, the individual meridians of astigmatism, in analogy to Lindner's cylinder-skiascopy. After complete correction of the error of refraction, the patient is offered a picture in which the slightest deviations from the correct value can be clearly recognized.

The duochrome-star test is considered a means of more refined testing of the spherical and cylindrical correction which already had been determined in other ways, whether subjectively or by means of objective methods.

In the case of a skiascopic value of +1.0 sph. = +0.5 cyl. axis 150, the test apparatus is employed as follows. First the spherical correction of one diopter

is placed before the eye—and the ground test glass is set at 150 degrees, i.e. the meridian determined by skiascopy. If this meridian actually corresponds with the axis of the astigmatism then the patient sees the main double-lines as sharp lines while the secondary double-lines are equally blurred. If the axis of the astigmatism lies outside of this meridian, one of both secondary double-lines will appear sharper than the other, and the test ground glass must be rotated in the direction of the sharper secondary double-line until both secondary double-lines appear in the same sharpness.

In case of astigmatism amounting to more than 1 diopter, the secondary double-lines are much too blurred for evaluation when the main double-lines are set in an approximately correct manner. The correct setting of the test ground glass can be recognized in this case from the sharpness of the main double-lines (strip) and from the sharpness of the short peripheral lines which are losing of their sharpness in proportion with their distance from the main double-lines on both sides. Furthermore an apparently bayonet-like break of the main double-lines occurs on the red-green border line when the test ground glass is not set correctly.

Comment: For many years refractionists have been intrigued by the possibility of using the normal chromatic aberration of the human eye in subjective and even objective refraction procedures. During the 19th Century the cobalt blue lens, still a part of many modern lens test cases, was actually used as a diagnostic test by many ophthalmologists. Since that time, many variations of the test have been introduced, but only one, the duochrome test in modern projection charts, is now used widely.

The author of this paper has not only revived the duochrome test in yet another form, but has combined it with a version of the oblique line axometer, of which the Lebensohn chart is the most useful representative.

In common with many other ophthalmologists, I have had considerable experience with each of these techniques individually, but none with them in combination, and it would seem worthwhile for some qualified person to use the Duochrome-Star test experimentally to see just how well it would fit into refraction procedures in this hemisphere.

Theoretically, subjective procedures using ocular chromatic aberration assume that the normal refractive state of the eye is adapted to that part of the spectrum which contains the yellow D (sodium) line and which is about midway between the green and red. Actually, it has been shown that some individuals prefer to use frequencies which are away from the D line in either direction, and in these persons an equalization of the red and green chromatic blurs would not represent the frequency for which the refractive systems of their eyes are best adapted.

The second difficulty in duochrome tests is that of matching blurred rather than sharp objects or backgrounds. It takes a fairly high order of intelligence and cooperation to do this accurately, and thus the test is not uniformly efficient, although many who use it routinely recognize the difficulty and allow for it.

To some extent, the same objection, that of the difficulty of matching blurred objects, also pertains to the oblique line axometer portion of the test, but actually there are very few individuals who cannot indicate when the lines are approximately equal. As in all subjective tests, and also in many objective tests, the chief difficulty is not in the patient's judgment but in his aberrant accommodative reflexes, especially that of tonic accommo-

dation which may be excessive because of a ciliary muscle hypertonus or, and more rarely, lacking because of hypotonus.

Neither the duochrome nor any other subjective test will, by itself, reveal the existence of the latter conditions. For a definite diagnosis, a comparison of all available subjective and objective tests results is essential and each of them, including chromatic and axometer findings, must be interpreted in the light of its own limitations. With such a process, the results of these and any other accepted procedures will be usable and helpful.

EDWIN F. TAIT

THE INTRAOCULAR PRESSURE

IS BJERRUM'S SCOTOMA EXTRAOCULAR IN ORIGIN?

A. Dubois-Poulsen and C. Magis

Paris, France

Acta XVII Councilium Ophth., 1954, 1136–1144

Glaucoma may be clinically defined as an atrophic excavation of the papilla accompanied by campimetric changes and an increase in ocular tension. These elements are not all constant. The excavation may be lacking; the tension may be normal; but glaucoma cannot well be said to exist without changes in the visual field. Studies of the visual field characteristics should, therefore, form part of any investigation into its origin. One of the most important perimetric symptoms found in patients with glaucoma is Bjerrum's scotoma, which may be either a true scotoma, that is, a blind area surrounded by a normal field, or a depression of the middle isopters with baring of the blind spot.

Study of 112 glaucomatous patients by the latest photometric methods of perimetry showed that the pattern of the first variety, which is clear in outline and presents a perfect arch, is the kind found in glaucoma; it represents a neuroscotoma and is caused by a bundle defect. The pattern of the second variety, on the other hand, is rough; its borders are irregular, and it does not surround the point of fixation precisely. This curving pattern is the result of faulty irrigation of the retina by the curving vessels surrounding the point of fixation, and the scotoma is therefore an angioscotoma.

Bjerrum's scotoma is always negative, that is, the patient is never aware of its existence. Its development is almost always bilateral, spreading rapidly until it coincides with defects in the nasal areas of the fields. Some authors believe that the scotoma begins at the periphery and extends toward the blind spot; in reality, however, the opposite is true and when the testing is done closely enough, the scotoma will always be found attached to the blind spot. It often coincides with other field defects, especially those suggesting chiasmal lesions.

Furthermore, Bjerrum's scotoma is independent of the intraocular pressure; it does not always appear in the eyes that have the highest pressures, and it is not infrequently aggravated by fistulizing procedures. Often, too, the most extensive field defects are found in long-standing low-tension glaucoma. The scotoma may exist in glaucoma without increased pressure, especially in de Graefe's disease. A reduction in intraocular pressure, however, may ameliorate it, but it will not cause it to disappear completely. Two elements, in fact, seem to exist in the glaucomatous fields, in which a general lowering of the thresholds is accompanied by a concentric contraction of the isopters that is apparently due to the ocular hypertension and also by localized defects that are more properly the characteristics of the glaucoma. The lowering of the thresholds

aggravates both the contraction of the isopters and the localized defects, but these elements are to some extent independent of one another and suppression of one does not necessarily lead to the disappearance of the other.

Similarly, Bjerrum's scotoma is independent of the cupping of the discs. Changes may be brought about in it by various pharmacodynamic influences. Thus the ingestion of water, caffeine, and accumulation of respiratory carbon dioxide increase it, while oxygen inhalation decreases it. It is also decreased, at least in the beginning, by instillations of pilocarpine, and this is a fact of great diagnostic importance.

Finally and very importantly, Bjerrum's scotoma is not pathognomonic of glaucoma; it may, in fact, be found in many lesions affecting visual pathways anterior to the lateral geniculate body: vascular lesions of the retina, choroiditis, myopic choroidosis, optic neuritis of inflammatory or toxic origin, tabes, retrobulbar neuritis, optic neuromyelitis, neuritis caused by sinus infection, trauma of the optic nerve, Leber's disease, chaismatic tumors, and optochiasmatic arachnoiditis. It has even been found in a case of parieto-occipital astrocytoma, in two cases of parieto-occipital trauma, and one of occipital shell wound. This ubiquity of Bjerrum's scotoma suggests that it corresponds to a clearly distinguishable bundle of nerve fibers.

The question then arises: Is the lesion responsible for the scotoma to be found in the globe, or does it occur outside it at some point in the bundle? The weight of the evidence seems to show that it is both extraocular and vascular in origin, but the exact site of the extraocular lesion is still uncertain. It may be located immediately posterior to the eyeball in Haller's arterial circle (Beauvieux) or further back in the optic nerve. In this connection, recent studies relating to sclerosis of the pial sheath of the nerve should be taken into account.

Verification of these hypotheses would mean that one of the most important signs of glaucoma is unrelated to intraocular pressure, and that studies dealing with the anterior chamber angle, the pressure, the flow of liquid, and the globe in general pertain only to a part of the pathogenic problem presented by this disease.

Comment: The conclusions of Dubois-Poulsen and Magis in regard to the Bjerrum scotoma are important in that they indicate the lack of specificity of the scotoma to glaucoma and that the cause is vascular. Although the authors always found the Bjerrum scotoma to be connected to the blind spot, others have described the scotoma as occurring separately (Traquair, van der Heove, Peter, Sloan and Blaxter). This would suggest that it is not due to a nerve fiber bundle lesion but rather a vascular one.

These conclusions suggest that progression of the scotoma in the presence of increased intraocular pressure is due to vascular embarrassment. It would also fit into the idea of a continuing vascular lesion in the optic nerve occurring coincidentally with the increased resistance to outflow of aqueous humor in the anterior portion of the eye.

Against the idea of the Bjerrum scotoma being extremely vascular is the extention to the raphe and its widening as it extends. These indicate nerve fiber involvement. The reviewer would rather consider the Bjerrum scotoma to be of combined vascular-nerve fiber origin, the vascular effect predominating early, the nerve fiber involvement, later.

H. Saul Sugar

GONIOTOMY FOR GLAUCOMA ASSOCIATED WITH NAEVUS FLAMMEUS: SUCCESSFUL OPERATION IN TWO CASES

Otto Barkan

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Glaucoma associated with naevus flammeus (encephalo-oculo-cutaneous angiomatosis) in infants and children often passes unnoticed for several years; occasionally, however, these patients show changes characteristic of congenital glaucoma or buphthalmos. In later years, the course of the disease is similar to that of open angle (chronic simple) glaucoma in the adult. The surgical treatment of this condition has hitherto been disappointing: some cases are arrested, a few respond to treatment, but the final result in most is absolute glaucoma ending in blindness. For this reason, any procedure that can be safely used to reduce the intraocular pressure and so preserve the vision deserves consideration.

Goniotomy under gonioscopic control was tried in two patients, a 10-year-old girl and a 6-year-old boy. In two eyes, the pressure was brought back to normal and has remained so for 16 months and 2½ years, respectively. In a third eye treated by this procedure, the pressure was reduced, but only temporarily. Two cyclodialyses and two cyclodiathermies have also failed to bring the pressure down to a normal level in this eye.

The three principal theories advanced to account for the increased intraocular pressure in glaucoma associated with naevus flammeus are the vascular (hemangioma of the choroid); the nervous (abnormality of sympathetic innervation); and the mechanical (developmental abnormality in the chamber angle). Although the first of these is the one most commonly accepted at the present time, the findings in these patients support the theory of mechanical obstruction. Preoperative gonioscopy in each case showed the angle to be filled and the angle wall covered to a varying extent by tissue that resembled iris stroma in appearance. There was an anterior insertion of the iris. Gonioscopy after the operation showed a partial removal of the aberrant tissue which covered the angle wall. There was no sign of incision of the angle wall, of external fistulization, or of communication with the suprachoroidal space to account for the reduction of pressure. The retention and glaucoma must have been due to obstruction of the angle by aberrant tissue, a conclusion which favors the mechanical theory. The angiomatosis which was present did not appear to have any causal relationship with the increased pressure in these eyes.

Since goniotomy under gonioscopic control is without hazard, it may be considered the operation of choice in cases of glaucoma associated with naevus flammeus in which gonioscopy shows an obstructive anomaly in the chamber angle. It produces no disfigurement. It preserves a round, central, freely reacting pupil. If the first procedure does not normalize the pressure, it can be repeated

on adjacent sections of the angle. Furthermore, it does not interfere with the performance of any secondary operation that may be required. In this condition, however, as in so many others, the importance of early diagnosis and early operation cannot be overemphasized.

Comment: Barkan's belief that the normalization of tension by goniotomy in 2 cases is an indication that a developmental anomaly is responsible for the glaucoma is certainly reasonable in these two cases. However, cases have been reported, including some cited by Barkan in which the angle is normal. Here one would more reasonably look for a hemangioma in the choroid, and probably an increased rate in aqueous formation. Enough histologic evidence for such cases with hemangioma has been shown. One would therefore, expect that goniotomy would be effective in those cases where a congenital anomaly of the angle exists but not where the angle is normal.

H. SAUL SUGAR

THE LENS

CONTRIBUTION TO STUDY OF OPERATION OF CATARACT

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Acta XVII Councilium Ophth., 1954, 86–99

The use of curare in cataract surgery and the preoperative medication resulting in hibernation facilitate the operation of cataract. The two steps of akinesia of the facial nerve and the retrobulbar injection are eliminated. Curare is not dangerous to the patient. Barraquer's technique is used as follows: Prior to the operation, 9 mg. of d-tubocurarine chloride is diluted in 3 cc. of sodium chloride solution. The injections of this solution are given slowly in the vein of the patient's arm, in a dose of 1 cc. of the solution (3 mg. of curare) for each injection. Each injection of 1 cc. of the solution should take a minute. The first injection is given before starting the operation. It causes paralysis of the ocular muscles which appears 2 minutes after the injection and lasts for 30 minutes. If the upper eyelid does not close and muscular relaxation does not occur within 2 minutes after the first injection, a second injection is given. Only in rare cases is a third injection of the last 3 cc. of the solution (which would make a total dose of 9 mg. of curare) necessary. Prostigmine and atropine are the antidotes of curare. If any alarming disorders of respiration occur, as a result of the administration of curare, an intravenous injection of from 3 to 5 mg. of prostigmine, or of 2 mg. of atropine dissolved in 2 cc. of sodium chloride solution, will automatically control the symptoms. The intense degree of muscular relaxation that curare produces in all the muscles of the eye eliminates the danger of the loss of vitreous, which is especially serious when the operation is performed on highly myopic eyes or when the lenses are luxated.

Hibernation produces in the patient a torpid lethargic condition. Luminal and phenergan are given 12 hours before the operation and luminal, phenergan and demerol 1½ hour before. These three drugs because of their hypnotic, sedative, anti-allergic and anti-histamine action produce a deep, quiet and tranquil sleep in the patient, but, in reality, the patient is in a true medicamentous coma, being unconscious, insensible to pain and incapable of waking during the operation.

Other important and necessary stages of the operation are the following: (1) anesthesia of the cornea; (2) inducement of ample mydriasis; (3) corneal section with Graefe's knife; (4) placement of corneo-corneal sutures; (5) preparation of the second knot of the threads used in the sutures and (6) iridotomy or iridectomy. Corneal anesthesia is induced by means of instillations of a 5% cocaine solution, repeated several times at short intervals before the operation. Ample mydriasis is attained by injecting 4 or 5 drops of a 1:1000 adrenalin

solution into the bulbar conjunctiva near the limbus at a point at 6 o'clock, with a fine needle. The corneal incision is made at a distance of 1 mm. in front of the limbus, following the line of the arcus senilis. By following this line, injury to the blood vessels near the limbus and postoperative hemorrhage at the anterior chamber are prevented. Non-perforating corneo-corneal sutures are made with the Grieshaber needle 82/7 (Barraquer's model). The first two stitches are placed at 1 o'clock and 11 o'clock respectively, in order to leave the field around 12 o'clock free from any stitches or threads, as it is at this point that the Arruga or Castroviejo's forceps is introduced to seize the lens. In closing the corneal wound, the second knot should be left easy to untie, because it is to be removed from the field, 10 days after the operation, without offering the risk of opening the anterior chamber. Small iridectomy is made by the Hess's method.

The four pitfalls to be avoided during the operation are: (1) The narrow pupil, which is avoided by performing the operation only when a good mydriasis has been induced by the injection of adrenaline solution (as previously detailed). (2) Rupture of the anterior capsule and (3) luxation of the lens are avoided by making the extraction of the lens near the equator of the lens, as this is the point in which the capsule is stronger and the fibers of the suspensory ligament are the most fragile. (4) Loss of vitreous during the operation is prevented by the use of curare, which causes intense relaxation and paralysis of the four rectus muscles of the eye. When these muscles are in normal tonus they cause pressure on the ocular globe leading to expulsion of the vitreous. The use of curare and hibernation and the technique followed, as previously explained in detail, also prevent the postoperative complications which may otherwise occur in operations of cataract, namely: hemorrhages of the anterior chamber, iritis and iridocyclitis, detachment of the retina and glaucoma.

Comment: Despite the fact that curare was first introduced by Dr. Kirby in this country approximately ten years ago, it would appear to have gained more popularity in foreign countries than it has in America. This may be due to the fact that most hospitals today have a well-qualified department of anesthesia and most ophthalmologists are a little wary of giving an intravenous drug such as curare without having an anesthetist present, or it may be due to the fact that American ophthalmologists feel they can obtain adequate sedation and control of the patient without curare. With the preoperative medication suggested by the author and the use of curare his patients are veritably rendered insensitive as well as insensible. The author states that they are in a true coma. This is not always a desirable state, especially in elderly patients. The operative procedure that the author recommends is fairly standard and every surgeon, whether he be the occasional operator or not, tries to avoid the pitfalls mentioned by the author. With the analgesics and anesthetics available today, there is no excuse for a surgeon's blaming any fault of the operation on the fact that the patient moved or was uncooperative. Should additional sedation be required during the operative procedure, this can usually be accomplished by the administration of intravenous sodium seconal or if the operation has not progressed to the stage where it can be stopped, the case may be cancelled and done at another time under general anesthesia with sodium pentathol.

P. Robb McDonald

THE PATHOLOGY OF EXPULSIVE HEMORRHAGE

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Expulsive hemorrhage in five of six cases previously reported by the author was due to rupture of a necrotic posterior ciliary artery. Since these eyes all showed severe glaucoma, the conclusion was drawn that glaucoma is capable of causing vascular necrosis, especially in the posterior ciliary arteries. Proof that degeneration of the vascular wall was present before the hemorrhage was obtained on examination of three eyes which were enucleated immediately after the hemorrhage. Anatomical study of four additional eyes shows, however, that glaucoma is only one of the conditions responsible for the occurrence of an expulsive hemorrhage.

The first patient was an 85-year-old man suffering from generalized arteriosclerosis. His blood pressure was extremely low, and this may have contributed to the occurrence of an ischemic vascular necrosis. The other three patients were women, aged 70, 68, and 71 years respectively, and all had decided hypertension. In none of these patients could any sign of glaucoma, either clinical or anatomical, be found. Clearly, then, intraocular vascular necrosis may be due to causes other than glaucoma. It may be part of a generalized arteriosclerosis, as in the first case, or of vascular hypertension, as in the other three.

The suggestion has been made that the necrosis is the last stage of an allergic-hyperergic injury to the vascular mesenchyma. This view, however, does not explain why the vascular necrosis within the eye is often more severe than it is elsewhere in the body. Moreover, the findings in the first and fourth cases showed that the necrosis can occur in patients without any indication of nephritis and consequently without any allergic-hyperergic vascular mesenchymal injury.

A factor always neglected in consideration of the pathogenesis of intraocular vascular necrosis is the normal intraocular pressure. This "normal" extravascular pressure within the eye, however, is 20 to 25 mm. Hg higher than the atmospheric extravascular pressure elsewhere in the body, except for the intracranial pressure, which is 10 to 12 mm. Hg higher than the atmospheric pressure. The blood pressure in the intraocular arterioles may be estimated at about one-half the diastolic blood pressure, while the blood pressure in capillaries is about one-sixth the diastolic blood pressure. Inasmuch as fluid can flow through a collapsible tube only so long as the fluid pressure inside the tube is equal to or greater than the sum of the pressures exerted externally on that tube, it is easy to see that the increase in the extravascular pressure within the eye must have a definite effect on the quantity and the speed of the blood that passes through the arterioles. It has long been known that slowing of the peripheral plasma of the blood column within a vessel causes a derangement of the metabo-

lism of the vessel wall, and that arteriosclerosis must be considered a direct consequence of this derangement ("angiomalacie").

The nutrition of a vessel wall is accomplished by (1) the penetration of plasma constituents through the endothelium, (2) the vasa vasorum, and (3) penetration of extravascular tissue fluid. Since the arterioles do not possess vasa vasorum, the nutrition of the arteriolar walls can be accomplished only by penetration of fluid from inside and outside the vessel wall. These two streams do not come from opposite directions to meet somewhere in the media; on the contrary, there is a diffuse penetration of the vessel wall with nourishing fluid, and this fluid is ultimately discharged into the perivascular tissue and not into the vascular lumen. Experiments have shown that any factor that impedes this intramural fluid circulation causes degeneration of the vessel wall. In the case of intraocular vascular degeneration, these factors may be (1) vascular hypertension, causing arteriolar sclerosis, (2) general arteriosclerosis, both by means of the structural changes in the arteriolar wall and by means of a reduced passage of blood through the vessel, and (3) the intraocular pressure, because an increased extravascular pressure within the eye hampers the outflow of the circulating intramural fluid and reduces the passage of blood through the vessel.

The fact that the extravascular pressure within the eye is higher than it is elsewhere in the body explains why the vascular degeneration within the eye is also often more severe than it is elsewhere in cases of general vascular disease. In addition, it explains why the intraocular vascular degeneration is located preferentially at the point where the vessels enter the eye, that is, where they pass from the atmospheric extravascular pressure into the intraocular extravascular pressure. The most convincing argument in favor of the importance of the extravascular pressure as a cause of intraocular vascular necrosis, however, is that provided by the occurrence of such necrosis in patients with glaucoma who show no signs of high blood pressure or generalized arteriosclerosis.

Comment: Expulsive chorordal hemorrhage is a complication feared by most ophthalmic surgeons. Fortunately, the incidence of its occurrence is very low. One can seldom prognosticate as to when it is going to occur and there is little one can do about it when it does occur. An immediate sclerectomy with evacuation of the hemorrhage through the sclera would appear to be the only procedure available. Unfortunately, the author is not able to help us in the preoperative selection of cases.

P. Robb McDonald

THE OCULAR MUSCLES

SYMPOSIUM ON STRABISMUS: SURGERY AND ORTHOPTICS

Am. Orthoptic J., 1955, *5:* 5–34

Addressing the Annual Joint Meeting of the American Orthoptic Council and the American Association of Orthoptic Technicians, Edmund L. Cooper, of Detroit, Michigan, stated that strabismus cannot be said to be functionally cured unless (1) no tropia is shown by the cover test either for distance or near; (2) the patient is able to fuse Worth's four dots both for distance and near; (3) the patient is able to fuse with a red glass before one eye both for distance and near; (4) visual acuity is equal, or nearly so, in each eye; and (5) there is no incomitance. To be more thorough, one might add the requirements of bar reading, physiologic diplopia, fusion with amplitude, a near point of convergence of at least 100 mm., and fusion and clear vision on the Remy separator.

These standards have been used in evaluating 333 cases of comitant esotropia and 77 cases of comitant exotropia, all of which were first seen between June, 1945, and January, 1954, and in all of which operation was eventually performed. Cases of accommodative esotropia and some cases of intermittent exotropia which were satisfactorily cured with refraction and orthoptics alone are therefore not included in the series.

The percentage of functional cures is higher when surgery is performed early. In comitant convergence, strabismus surgery before the age of 6 years results in good function. After 6, functional cures are obtained in most cases only with the aid of orthoptic training. The older the patient, the less chance there is of success, whether orthoptic training is given or not. Comitant divergent strabismus may be cured functionally at any age, and there seems to be no reason for urging early operation for fusional purposes alone. Other factors, such as psychological trauma, increase in exotropia with time owing to an increasingly divergent position of the orbits, or a lessening of accommodational tone, may justify early surgery in patients who do not respond to orthoptics. Surgery should be performed as soon as it is apparent that the exotropia is becoming constant.

When surgical correction is undertaken, the goal should always be proper alignment of the visual axes without incomitance and without impairment of convergence ability. For this reason, it should be carried out symmetrically and great care should be exercised in recessing the medial recti when there is a poor convergence near point. Success in the treatment of nonaccommodative comitant strabismus depends essentially on adequate and complete cooperation between the ophthalmologist and the orthoptic technician, the former correcting the deviation and the latter providing the necessary sensory background on which fusion may be established. Given an otherwise healthy, intelligent, and cooperative patient, failure to cure a squint satisfactorily is due either to the surgeon's failure to abolish the deviation, horizontal or vertical, or to the failure

of the orthoptist in helping the patient to overcome the anomalous correspondence and amblyopia.

Discussing the criteria for orthoptic training before and after operation, Nancy M. Capobianco, New York, New York, said that comfortable monocular vision should not be disturbed if the attainment of comfortable binocular vision appears unlikely. It is a mistake to assume that every patient with strabismus should have orthoptic training. The purpose of preoperative training is to establish normal visual habits; it should overcome amblyopia ex anopsia, develop steady monocular fixation with each eye, eliminate suppression, make the patient aware of diplopia, and finally develop fusional amplitudes. Equal visual acuity is essential to normal binocular vision; consequently, there can be no halfway treatment in regard to amblyopia, and occlusion should be continued to the time of surgery. Normal fusion cannot take place if fixation with each eye does not exist. If occlusion alone is not enough to change the fixation pattern, it must be supplemented by fixation training. Diplopia training should be given only in selected cases, but training on the major amblyoscope, which is used to eliminate suppression and to reawaken and stimulate fusion, should be started while occlusion and fixation exercises are being continued. The time required for preoperative orthoptics varies with the patient and the clinical findings. If further progress is prevented by some obstacle, surgical treatment should be undertaken without delay. Similarly, anomalous correspondence should not usually be accepted as a reason for delaying surgery in patients with equal visual acuity and steady fixation. If the patient appears to have unstable anomalous correspondence after operation, orthoptic treatment can be given then.

Just as the aim of preoperative treatment is to establish normal visual habits, so the postoperative treatment is aimed at stabilizing these habits to permit the development of steady fusional control. After surgery, the sensory and motor apparatus is undergoing a readjustment. Much can be done for the patient at this pliable stage, and the orthoptic training at this period should be intensive. Office visits and home training may be gradually decreased as the patient progresses, but occasional checkups should be made to see that the successful result is maintained. If the patient shows a tendency to revert to bad visual habits, he can then be given a refresher course.

The next speaker, J. R. Anderson, Melbourne, Australia, whose remarks were devoted to surgery for strabismus, emphasized the vital importance of preventing amblyopia. The records of 350 patients with convergent squint, with follow-up until they could read, showed that 24 per cent had vision of 6/18 (20/60) or less in one eye. Only 10 per cent of those with onset of squint before 2 years of age had, in the opinion of the orthoptist, received adequate occlusion by the age of 4, and of those with squint arising between the ages of 2 and 4, only 20 per cent had had adequate occlusion by the age of 6 years. One problem is the relatively late age at which advice is sought; although the average age at onset for 352 patients with convergent strabismus seen by the author was 2.14 years, the average age at which they reached him was 5.7 years.

Next in importance comes inadequate correction of hypermetropic errors. Four out of every five convergent squinters are hypermetropic, while only four of every 100 are myopic. This suggests the possibility that hypermetropia must be removed if strabismus is to be eradicated. Nothing simplifies future treatment so much as early and full correction with glasses. The preventive value of early full correction of refractive errors far outweighs the partial curative effect of stronger glasses ordered later. In spite of the good results that can sometimes be obtained with glasses and occlusion alone, however, therapeutic orthoptics should not be dispensed with, because the range of fusion, of accommodation, and of motility may be improved.

In nonaccommodative squint in which the deviation is reduced by glasses by less than 75 per cent, the influence of both innervational and structural factors should be carefully estimated in each case. Obviously, it is useless to expect orthoptic training to alter structural defects or to produce fusion when the ability to fuse is absent.

Lorna Billinghurst, Cambridge, England, laid particular stress on the investigation and treatment of those cases of strabismus and heterophoria in which surgery is contemplated. The orthoptist's role in the treatment of strabismus is both diagnostic and therapeutic. First, it is necessary to diagnose the type of deviation and, when applicable, the extraocular muscle palsy or overaction involved; then an assessment must be made of the grade of binocular vision present and the degree to which binocular function has become disturbed by the onset of a squint. Finally, a prognosis must be given. The therapeutic intention is to prevent abnormal sensory adaptation to the changed ocular posture and to re-establish normal sensory function if changes have already been produced by the motor abnormality.

In those cases of convergent squint in which the sensory pattern has not yet been disturbed sufficiently for secondary changes to have taken place, orthoptic training aims at ensuring the maintenance of equal visual acuity, and occlusion is carried out, when necessary, in cases of unilateral squint. In the cases in which surgical treatment is necessary, the operation aims at making the visual axes parallel or a few degrees convergent.

When the sensory pattern has already become abnormal, orthoptic training must be directed first to the elimination of amblyopia ex anopsia, if it is present. Visual acuity is not easy to estimate in a child under three years old but he can be treated for amblyopia if he finds it impossible to maintain fixation with the deviating eye when the cover has been removed from the fixating eye. When amblyopia is intractable, as it may be in any age group, surgery is planned to leave the patient with up to 10 degrees of residual convergence, allowing for physiological divergence to take place with the passage of time.

It is generally agreed that established abnormal retinal correspondence never responds to orthoptic treatment, and treatment is given only as a diagnostic measure when the state of binocular correspondence is open to doubt at the first examination.

Many factors in the etiology of strabismus are still obscure, both as regards the onset and the various ways in which the sensory pattern is adapted in the

face of an existing deviation. Further advances must depend on the coordination of research in many fields.

Comment: These important papers should be read in conjunction with that of Ronne's concerning fusion in the optics section of this issue, with particular attention to the comment by Dr. Linksz. The importance of preventing the development of amblyopia ex anopsia is emphasized as the most fundamental step in the treatment of squint. In doing this there is nothing superior to constant occlusion of the non-amblyopic eye. The use of occluders attached to the spectacle frame, opaque lens coatings, cycloplegics, and similar devices to discourage use of the eye should be limited to those children in whom constant occlusion cannot be initiated immediately. It is most unfair to a child, however, to neglect constant occlusion because he removes the patch, has tantrums or demonstrates the other stratagems that mothers report when the child is the dominant member of the pair. The prevention of amblyopia is so important that it is well to insist upon proper treatment even at the risk of damage to the child's psyche. For the most part, the teachers, psychologists and psychiatrists who oppose this view have never had to treat a patient who had lost his "good" eye.

The difference in viewpoint which exists in orthoptics groups is well borne out in several parts of these papers. Some believe that binocular fusion can be developed in all individuals and that anomalous correspondence can be corrected while others feel that patients without fusion or with anomalous correspondence will not respond to orthoptic management. It is unfortunate that a confusing terminology and even disagreement concerning the fundamental physiology involved prevents objective analysis of the results already obtained. If anomalous correspondence can be successfully treated what criteria should be used for the diagnosis and correction? Why should treatment for this be more successful in the United States and The Netherlands than in England or Australia? The presentation of a careful analysis combined with appropriate controls of such cases would be most interesting.

The emphasis upon symmetrical surgery is becoming more widely accepted. The monocular recession-resection operation is being increasingly limited to amblyopic eyes and even here the tendency is toward bilateral lateral rectus resections or, more rarely, medial rectus recessions.

DISTURBANCES OF EYE MOVEMENTS AS A NEUROLOGIC PROBLEM

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New England J. Med., 1956, *254:* 461–464

The physician called upon to make a diagnosis in a patient with disturbances of eye movements must first determine whether the disturbances are the result of mechanical factors or whether they are caused by a disorder of innervation.

Purely mechanical impairment of ocular motility depends on local factors and lies outside the scope of the present discussion. Neurogenic disorders of eye movements, on the other hand, rarely originate in the eye itself, but are usually due to a lesion (or lesions) in the nervous system; consequently, in such cases, a detailed neurologic examination becomes necessary.

The extraocular muscles are innervated by a complex multineuronal system. Its function may be understood by comparing the innervation of the eye muscles with that of other striate muscles: the peripheral link in the neuronal chain, the so-called lower motor neuron or common terminal pathway, is formed by nuclei, roots, and peripheral fibers of the third, fourth, and sixth cranial nerves, in analogy to the spinal anterior-horn cells, motor roots, and peripheral motor nerves. The activity of the lower motor neurons for the eye muscles is controlled by an "upper motor neuron" system in the brain stem and cortex. Its role is comparable to that of the so-called pyramidal and extrapyramidal systems.

A fundamental difference in the supranuclear control of eye movements from the analogous supraspinal control of limb muscles lies in the fact that the innervation of eye muscles represents a closely coordinated pattern of linked binocular movements, whereas the motor innervation of extremity muscles possesses a high degree of autonomy and flexibility. Figuratively speaking, the eyes are like a team of horses that, controlled by the reins of a determined driver, are permitted to perform only certain joint actions (such as lateral and vertical turning, fixation and centering movements).

The function of the neural network subserving eye movements is regulated by reflex impulses derived from various levels of the nervous system: visual, vestibular, and kinesthetic-proprioceptive stimuli constantly activate, inhibit, or modulate the peripheral responses. Thus, the intimate connections of the oculogyric apparatus with many other parts of the neuraxis explain the frequency with which lesions of the nervous system may affect eye movements.

When the nerve for a peripheral eye muscle is damaged by an extracerebral lesion, paresis or paralysis of the affected muscle or muscles ensues, and, owing to the pull of the prevailing antagonist, strabismus develops, in turn causing diplopia. The patient tends to eliminate double vision either by closing one eye or by turning the head in the direction in which the paralyzed muscle pulls—for example, the head is turned to the left when the left sixth nerve is paralyzed. Because the eye-muscle nerves take a long and vulnerable course along the base of the skull and orbit, passing through the subarachnoid space filled with cerebrospinal fluid, they are easily damaged by an adjacent local lesion. The examiner's first task is therefore to investigate all structures in the region of the affected nerve. Roentgenographic examination of the skull, with special views of the orbit, paranasal sinuses, petrous bones, and base of the skull, is extremely important here. Additional information may be gained by roentgenologic contrast methods, such as angiography and pneumography, and by examination of the cerebrospinal fluid.

The mere presence of a third nerve paralysis strongly suggests a focal process, and when the oculomotor palsy is accompanied by paresis of other adjacent

cranial nerves, the underlying lesion can be still more accurately localized. For example, combined involvement of the second and third cranial nerves points to an anterior parasellar or sellar process. Whenever third-nerve paralysis develops acutely and is preceded by a sudden, severe headache or supraorbital pain, the possibility of an intracranial aneurysm must be considered. Occasionally, oculomotor palsy may be one of the manifestations of diffuse disease of the nervous system or of generalized systemic disease. Bilateral partial oculomotor pareses, especially with bilateral ptosis, increased by fatigue, must always arouse the suspicion of myasthenia gravis.

Paralysis of the fourth nerve is not so rare as is commonly supposed; in many cases, it is probably not even recognized. Paralysis of this nerve, which supplies only the superior oblique muscle and acts as a depressor of the globe, when the eye is in the adducted position, is most disturbing to the patient when he reads or descends stairs.

Sixth-nerve paralysis is by far the most common of all extraocular palsies. The sixth nerve has the longest course of all the eye-muscle nerves and is highly vulnerable to mechanical compression, as well as being easily affected by inflammatory or vascular disease in its neighborhood. For these reasons, isolated sixth-nerve paralysis has less significance for topical diagnosis than paralysis of the other eye-muscle nerves. Only when it develops as the very first sign of brain tumor before symptoms of increased intracranial pressure have appeared can it be considered evidence for localization; it has no diagnostic value when it appears late.

The characteristic feature of a supranuclear disturbance of eye movements is the inability to perform conjugate eye movements in one direction, either in the horizontal or in the vertical plane. When the paresis of gaze is incomplete, the patient may be unable to sustain or to attain the end position, and consequently both eyes tend to float slowly back toward the zero position and to move back toward the end position on renewed effort. Thus, slow nystagmoid movements result.

The brain stem contains important mechanisms for eye movements, such as the nuclei and roots of the eye-muscle nerves and a complex integrating system, the most important component of which is the medial longitudinal fascicle. Lesions of the tegmentum of the midbrain, therefore, frequently produce a combination of lower-motor-neuron paralysis and supranuclear involvement of extraocular muscles. The following syndromes can be clinically recognized: (1) A lesion of the lower pontine tegmentum causes a combination of (nuclear) sixth-nerve paralysis and (radicular) involvement of the seventh nerve, with supranuclear paralysis of gaze to the side of the lesion; (2) lesions of the medial longitudinal fascicle at the floor of the fourth ventricle usually produce supranuclear paresis of the medial rectus, with paretic nystagmus of the opposite lateral rectus; and (3) lesions in the upper portion of the midbrain produce a combination of partial nuclear palsy of the third nerve and paralysis of upward and sometimes also of downward gaze. The nuclear involvement accounts for the pupillary areflexia and the paresis of the medial rectus.

Lesions of the cerebellar system may lead to asynergia, ataxia, and dysdiadokokinesis of eye movements, while in the Parkinsonian syndrome the eye muscles may participate in the generalized rigidity and characteristic slowing of spontaneous movements.

Two important cortical areas in each cerebral hemisphere, one in the posterior frontal region and one in the occipital lobe, are concerned with the initiation and control of eye movements. Stimulation of these areas of the kind that occurs spontaneously in certain focal seizures evokes turning of the eyes to the opposite side. A destructive lesion of the same area, however, leads to paralysis of gaze to the opposite side, frequently observed in an acute cerebrovascular accident.

Neurologic analysis of abnormal eye movements often gives valuable information concerning both the localization and the pathologic anatomic nature of an underlying disease process. Accurate diagnosis and effective treatment, however, require close cooperation between the neurologist and the ophthalmologist, or better still, evaluation by one skilled in both fields.

NEUROLOGY

ON THE LOCALIZING VALUE OF THE FOSTER KENNEDY SYNDROME: OBSERVATIONS ON ONE RARE CASE OF "INVERTED" SYNDROME

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The Foster Kennedy syndrome, retrobulbar optic neuritis, with central scotoma, or primary optic atrophy on the side of the lesion and papilledema on the opposite side is not always linked to the presence of an intracranial tumor, nor is the intracranial tumor always located near the frontal lobe on the same side as the optic atrophy as Foster Kennedy stated back in 1911. Since that year, seven cases of "inverted" syndrome have been reported in the literature. The lack of value of the Foster Kennedy syndrome alone in the localization of intracranial tumors is further illustrated by the eighth case of "inverted" syndrome.

A 51-year-old woman was seen with disturbances of the left, and later of the right, eye which appeared two years prior to the time of the first consultation. At this time, a diagnosis of Foster Kennedy syndrome with optic atrophy in the left eye and papilledema in the right was made. Perimetrically there was a left homonymous hemianopsia. The electroencephalograms revealed anomalies in the right anterior temporal and frontal region; the roentgenograms showed decalcification of the posterior sella and a calcified pineal body was displaced to the left; an arteriogram of the left side revealed no anomaly whereas one of the right side revealed a tumor of the temporal pole which had probably extended toward the frontal lobe. She was referred to a neurosurgical clinic, and at the time of admission she had .5 vision in the right eye, whereas with the left eye she could count fingers at a distance of 20 cm. Neurological examination revealed probable hyposmia on the right side, deficit of the lower facial nerve on the left, slight hyposthenia of the lower extremities on the left, a tendency of the patient to fall to the left in forward ambulation, and left hypodiadokokinesia.

Despite the fact that the neurological and ocular findings suggested that the tumor was located on the left side, on the basis of the arteriograms, intervention was performed on the right side. A meningioma (half the size of a chicken's egg) of the small wing of the right sphenoid bone was removed. The patient was discharged 13 days after the operation, at which time the papilledema in the right eye had begun to disappear as had the neurological symptoms, with the exception of a slight accentuation of reflexes on the left side. Follow-up

examinations two and six months later showed that the vision in the right eye had improved (she had almost 1.0 vision) and that there was also a slight subjective and objective improvement in the function of the left eye.

On the basis of this improvement, the author states that the left optic atrophy was undoubtedly linked to the tumor. However, the correct diagnosis of the location of the tumor was possible on the basis of the roentgenographic, arteriographic, and electroencephalographic findings. Had the location of the tumor been determined only on the basis of the presence of the Foster Kennedy syndrome, the diagnosis would have been completely erroneous.

Comment: It is not surprising to find another paper dealing with the lack of value of the Foster Kennedy syndrome alone in localization of intracranial lesions. The occurrence of such optic nerve changes is only a part of the diagnostic picture in any case. In the typical meningioma of the olfactory region which is classical for this syndrome Bailey in his excellent book on *Intracranial Tumors* lists the following symptoms in their order of occurrence:

(1) Ipsilateral anosmia from direct involvement of the olfactory bulb.
(2) Ipsilateral primary optic atrophy from pressure on the optic nerve.
(3) Complete anosmia by involvement of the opposite olfactory bulb.
(4) Mental symptoms from compression of the frontal lobes of the brain.
(5) Contralateral papilledema due to increased intracranial pressure.

More important is the recognition by the clinician of the possibility of intracranial tumor at the time of first involvement of the ipsilateral optic nerve in what appears to be a retrobulbar optic neuritis with central scotoma. Once atrophy has occurred the nerve head is less capable of presenting choking, and any subsequent increase in intracranial pressure, from whatever cause, can produce papilledema only in the opposite nerve head.

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GLIOMAS OF THE OPTIC NERVE

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Gliomas, which are the commonest primary tumors of the optic nerve, occur predominantly in children and young adults. They usually originate within the intraorbital portion of the optic nerve but may extend proximally through the optic foramen to invade the intracranial portion of the nerve and the optic chiasm. In a few cases, multiple foci of neoplastic growth are present, with extensive involvement of both optic nerves, chiasm, optic tract, diencephalon,

and the adjacent frontal or temporal lobes. Some evidence of Recklinghausen's neurofibromatosis is found in a significant proportion of the cases.

It seems likely that all gliomas of the optic nerve are composed of small astrocytes and polar spongioblasts in varying proportions. Such tumors will probably continue to be designated as either polar spongioblastomas or astrocytomas, depending on the cell type that predominates.

If the glioma is confined to the intraorbital portion of the optic nerve, unilateral exophthalmos that is slowly progressive but almost always painless is the usual presenting symptom. There is no palpable intraorbital mass, and the exophthalmos cannot be reduced by pressure on the globe. Visual field studies usually show a complete loss of the ipsilateral field, with no abnormalities being detected on the opposite side. Ophthalmoscopic examination usually reveals either primary optic atrophy or papilledema. In a few instances, a neoplasm involving the nerve head has been visible. In small children, there may be practically complete loss of vision without the patient's being aware of the disability. Diplopia is a rare complaint. If intracranial extension has occurred, most patients will show varying degrees of the chiasmal syndrome and may have evidence of increased intracranial pressure. X-ray pictures of an enlarged optic foramen or of a necklike shadow resembling a gourd, extending from the body of the sella under the anterior clinoid process, indicate intracranial involvement. Stigmata of Recklinghausen's disease should be looked for in all patients suspected of having a glioma of the optic nerve or chiasm. Such patients seldom show all of the clinical manifestations of generalized neurofibromatosis. An abortive form of the disease is more usually encountered, with the patient having only a few café-au-lait spots on the skin. Occasionally, skeletal defects are found, such as scoliosis or congenital lesions of the long bones.

In children, the differential diagnosis of optic nerve gliomas confined to the orbit must include other forms of retrobulbar neoplasms, while such lesions as craniopharyngiomas, primary hypothalamic gliomas, Hand-Schüller-Christian's disease, and metastatic sympathicoblastoma must be considered when intracranial involvement is present. In adults, meningiomas, pituitary tumors, and arterial aneurysms must also be taken into account.

Surgical excision is the treatment of choice. The anterior orbital approach should be used only in cases in which the neoplasm is confined to the intraorbital portion of the optic nerve. All patients with clinical or X-ray evidence of intracranial extension, or both, should be treated by frontal craniotomy. Enucleation should be performed only if there is definite evidence of neoplastic invasion of the optic disk. Decompression of an optic foramen, roentgen therapy, and cerebrospinal fluid-shunting procedures are palliative measures which are worth while in certain cases. Prognosis is excellent if the optic nerve glioma can be adequately excised; survival rates up to 24 years have now been recorded for patients who received adequate surgical treatment. Even when intraorbital optic nerve gliomas have been incompletely excised, survival rates are usually measured in years, although the patient generally succumbs to intracranial extension. In patients with Recklinghausen's disease, however, the prognosis must be more guarded because of the possibility of associated cerebral gliomas.

The case of a 7½ year-old-girl who was still alive and free from symptoms six months after surgical removal of an optic nerve glioma led the author to restudy the findings in the case of a 3½-year-old Mexican boy who died after recurrence of a glioma with intracranial extension. In the first case, the girl's parents noticed that her right eye was prominent about one month before she was admitted to the hospital. She had experienced no pain and was unaware of visual impairment. Ophthalmological examination showed a unilateral exophthalmos on the right. Vision in the left eye was normal, while in the right she had only light and finger-movement perception. Extraocular movements were not restricted. Advanced papilledema was noted in the right fundus, while the left appeared normal. The remainder of the neurological examination was entirely normal. There were no café-au-lait spots on the skin, and no cutaneous evidence of Recklinghausen's disease in the parents or one other sibling. X-rays of the skull showed definite enlargement of the right optic foramen, as compared with the left. The sella turcica appeared normal. The tumor was discovered and removed under general anesthesia in August, 1954. Recovery from this operation, a right frontal craniotomy, was uneventful, but about six weeks later the right eye was enucleated because the tumor was believed to have invaded the nerve head. When last seen in February, 1955, she was free from symptoms. A right prosthesis was being worn, and the cosmetic appearance was satisfactory. Visual acuity in the left eye was normal, and the visual field remained full. The left fundus showed no abnormality.

Prominence of one eye was also the first symptom noticed by the parents of the boy. Three months later it was discovered that he could not see objects out of the left eye when the right eye was covered. There had been no pain, seizures, or vomiting, and the child's development had otherwise been entirely normal. Examination led to a clinical diagnosis of a left optic nerve neoplasm and at operation a few days later the tumor was found and removed. The child remained well for eight months but then was readmitted to the hospital twice in the same month. Intracranial exploration disclosed a tumor in the base of the left frontal lobe measuring 2 to 3 cm. in diameter and lying adjacent to the left side of the optic chiasm. Only a partial removal was carried out. The child regained consciousness, but died suddenly 24 hours after the operation. It now seems obvious that intracranial extension was already present at the time of the first operation. There was no family history of Recklinghausen's disease and no evidence of it was detectable at autopsy.

CAROTICOCAVERNOUS FISTULAS

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Caroticocavernous fistulas are manifested clinically by an easily recognizable symptom: pulsatile exophthalmos, which is associated with a bruit audible both to the patient and to the physician. During the period from 1925 to 1951, 24 patients with this condition were observed at the Johns Hopkins Hospital.

Fistulas of this kind are almost always due either to a skull injury or to the spontaneous rupture of a pre-existing aneurysm or a congenital anomaly of the carotid artery into the cavernous sinus. The traumatic fistulas in this series were 14 in number, but in large series the proportion may be three traumatic fistulas to one that is spontaneous. A parietal defect in the internal carotid artery in its intracavernous portion seems to be a predisposing factor in the development of fistula. Pregnancy, too, is an important element in the development of a spontaneous fistula; in from 25 to 30 per cent of the women with these fistulas, exophthalmos appears during the last half of their pregnancy or in the course of labor. Arterial hypertension during pregnancy may also lead to the rupture of a pre-existing aneurysm in the cavernous sinus.

Angiography makes it possible to study not only the anatomical cause of the fistula but also and especially its hemodynamics, sometimes disclosing arteriovenous fistulization in the upper part of the neck. The local changes in the internal carotid may vary from complete section of the vessel to a tiny opening hard to see even at autopsy. As a rule, however, the arterial orifice is from 3 to 6 mm. in diameter. In some cases of traumatic fistula a spicule of bone has been visible in the arterial lesion, and at times the injury may consist of several openings. The location of the lesion, which may be on the superior aspect, the internal aspect, or the external aspect of the vessel, does not seem to influence the extent of the exophthalmos or its occasional bilaterality. Whether or not it is bilateral depends, in fact, on the size of the communication between the two sinuses on either side of the sella turcica. In most cases, such communications are very small and this is responsible for the frequency (80 to 90 per cent of the cases) with which the exophthalmos appears on one side only. In the present series, 22 of the 24 patients had unilateral exophthalmos.

The principal symptoms of caroticocavernous fistulas are exophthalmos, pulsatility of the eyeball, and an audible bruit; they may appear immediately after the injury or not until months later. The range in this series was from 2 days to 9 months for those that were not contemporaneous with the injury. The "noise in the head," which is usually the first symptom to be noted, may precede the exophthalmos by several weeks. This delay between the two symptoms is due perhaps to the fact that the arterial lesion is temporarily blocked by clots or by

parietal edema and begins to function only when the clot is resorbed or the edema decreases. Paralysis of the extrinsic ocular muscles very rarely precedes the bruit, but when an arterial aneurysm exists, it is not infrequent. Exophthalmos, which is usually unilateral and almost always appears on the same side as the fistula, is very rarely absent. The protrusion of the eye may be progressive over a long period; in most cases, it is about 10 mm., although it may vary from a few millimeters to almost 2 cm. Pulsatility is the rule and can be observed in the dilated veins of the forehead and sometimes in those of the neck. Chemosis, headache, diplopia, and visual disturbances may also be present in varying degree.

Differential diagnosis is seldom difficult, requiring only the elimination of an orbital encephalocele, a thrombosis of the cavernous sinus, an orbital tumor, or, with the help of angiography, an intraorbital vascular affection.

In some cases, the protrusion of the eye and the intensity of the bruit are so slight that the patient considers the risk of treatment greater than the inconvenience they occasion. In the absence of infection, the condition may remain stationary for years; on the other hand, it may end in a fatal hemorrhage. Spontaneous cures occur in about 10 per cent of the cases. As a rule, however, in patients who survive, the bruit becomes intolerable and the function of the eye is impaired; fewer than 20 per cent of the patients retain accurate vision after some years of exophthalmos. Carotid-artery ligation, which is the treatment most used in the surgical correction of caroticocavernous fistulas, was carried out in 21 of the present series of 24 cases, with ligation of the primary carotid in 6; of the internal carotid in 8; and Dandy's operation in 9. A complete and permanent cure was obtained in 16 patients. Two patients became blind after operation; 2 suffered severe impairment of vision; and 1 became hemiplegic.

Comment: The striking appearance of the patient with a caroticocavernous fistula should be emphasized. In addition to the pulsatile exophthalmos and the bruit stressed by the authors, the type of congestion and chemosis is almost pathognomonic. Large, numerous injected conjunctival vessels are seen, and at times evidence of stasis appears on ophthalmoscopic examination. It is possible that visual loss following surgical treatment depends on the lapse of sufficient time for the development of increased collateral circulation to the ophthalmic artery through the external carotid connections. Two recent cases seen at the University of Michigan suggest such a mechanism. The first patient had carotid ligation in the neck followed by intracranial ligation after a lapse of several months, and vision remained normal. In the second, ligation in the neck and intracranially were performed at the same session, and the postoperative vision was poor. In most cases a history of antecedent head trauma aids in reaching the proper diagnosis. In an occasional case, the problem of corneal exposure with the acute exophthalmos becomes a major factor, and measures for protection should be instituted.

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THE ORBIT

MALIGNANT EDEMATOUS EXOPHTHALMOS TREATED BY HYPOPHYSECTOMY

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The problems presented by patients with malignant exophthalmos accompanied by severe ocular complications are often distressing and hard to resolve. Some authorities advocate orbital decompression; others believe that operation can usually be avoided by hypophyseal and orbital radiotherapy. The appearance of bilateral retrobulbar optic neuritis in a 56-year-old woman with malignant exophthalmos that had already been complicated by a subacute attack of glaucoma in the right eye led the authors to decide on total hypophysectomy as a life-saving measure.

The patient's troubles began with a mild edematous exophthalmos (20 to 22 by Hertel's exophthalmometer), associated with signs of pronounced hyperthyroidism: tachycardia with a rate of 120, a moderate but vascular goiter, decided trembling, loss of weight, and elevation of the basal metabolism to 65 per cent. Progressive reduction of the hyperthyroidism was obtained by resorting successively to synthetic antihypophyseal agents, hypophyseal radiotherapy, and finally thymic extracts, but in spite of this the exophthalmos increased until six months later it was practically irreducible, with a Hertel measurement of 24 mm. and 23 mm. Visual acuity was 8/10 in each eye. The patient was hospitalized in June and in July she had a subacute attack of glaucoma in the right eye, which had a pressure of 65 mm. Hg, as compared with 30 mm. Hg in the left eye. Under the influence of pilocarpine treatment, the glaucoma receded and the pressure in the right eye fell back to 25, but the state of the cornea made blepharorraphy necessary. In August, during exacerbation of the edema, the blepharorraphy gave way. A complete examination made the same day showed a bilateral decrease in visual acuity to 1/10 with a central scotoma for colors; the fundi examination showed that the discs were normal, but the arteries were sinuous. On September 8 the exophthalmos was 24 mm. on the right and 23 mm. on the left (Hertel); the visual acuity was unchanged, but the central scotoma, which remained relative on the right, had become absolute on the left. Before this alarming state of affairs from the visual point of view, the possibility of an orbital decompression was considered. But the patient's general condition was now poor; general manifestations of a toxic character had appeared, with fever unexplained by infection, supraorbital headaches so severe as to cause insomnia and torpor, facial emaciation accompanying a general loss of weight, and anorexia.

Prompted by Dobyns's recent discoveries, which point to the secretion of thyreotropin by a histologically altered hypophysis as responsible for the symptoms in malignant exophthalmos of this kind, the authors decided that hypophysectomy, which might prove curative, would be better than orbital decompression, which would be no more than palliative. The operation was performed on September 13, and improvement followed at once. The exophthalmos regressed to the point where it measured only 20 mm. (Hertel), as compared with the 24 mm. and 23 mm. of the preoperative readings. In January, 1955, the visual acuity on the right side had risen from 2 to 8/10, and that on the left had risen from 1 to 4/10; the central scotoma had disappeared, but the visual fields were somewhat impaired. The general syndrome that had accompanied the exophthalmos was also favorably influenced by the operation. The temperature returned to normal and the patient regained weight, but she still showed a complex endocrine syndrome, with a slight diabetes insipidus, requiring daily restitutive therapy of 15 mg. of cortisone, 2 cgm. of thyroid extract, and 10 units of posthypophysis powder.

The excellent results thus obtained by the hypophysectomy have been maintained for over 8 months, and the postoperative endocrine deficit can therefore be regarded as unimportant. Nevertheless, an operation of this nature should be undertaken only after very careful consideration of the operative indications and only in cases in which the general syndrome is such as to jeopardize the patient's life. Experience in future cases will show whether the indications can be broadened, or whether the operation must remain exceptional for patients with malignant exophthalmos.

Comment: During the past decade there has been a significant increase in the knowledge concerning the role of the endocrine glands in the production of the so-called malignant exophthalmos of Graves' disease. The finger of suspicion can now be reasonably well directed toward the pituitary gland as one of the main organs responsible for the development of this serious disorder of the orbit. It was to be expected, then, that physicians would either seek some medical means of suppressing the hormones from the pituitary gland that seemed to contribute to the hyperophthalmopathy or to invent some surgical procedure that would nullify their effect.

This editor feels that the above article is a significant one in that it represents one of the first clinical attempts to cure the malignant exophthalmos by surgical removal of the pituitary gland. The idea of surgical attack on the pituitary gland as a possible remedy for malignant exophthalmos is not new, however.

Ten years ago McCullagh, Ruedemann, and Gardner ("Exophthalmos of Graves' Disease Following Pituitary Irradiation, Orbital Decompression and Electrocautery to the Pituitary Gland." Trans. Am. Assn. for the Study of Goiter; 1946, pp. 15–32), gave an interesting account of four patients in whom a partial electrocoagulation of the pituitary gland was attempted as part of the program of treatment for severe asymmetric malignant exophthalmos. The electrocoagulation was confined to the area of the anterior lobe and the hypophyseal stalk. Since this surgery was also combined with the standard transfrontal decompression of one orbit, the resulting improvement in the exophthalmos could not be entirely credited to the procedure on the pituitary as the authors rightly pointed out. Furthermore, only one of the four patients developed signs of pituitary in-

sufficiency postoperatively so that there is, logically, some question as to how much effect the electrocoagulation actually exerted on the pituitary gland.

Still, at the time (the surgical procedures on these four patients were carried out in the period 1937–1946) these procedures were attempted it represented a bold and brave attempt to get at the theoretical seat of the disorder. During this period of 10 to 20 years ago the majority of physicians, as well as physiologists, would have been hesitant to recommend any surgically destructive procedure on the pituitary gland because of the fear of the metabolic consequences (as occurred in one of the cases reported by McCullagh, Ruedemann, and Gardner). Most of us were thoroughly indoctrinated with the idea that the pituitary gland was the leader of the hormone orchestra and, therefore, considered this gland well nigh indispensable.

It was a rude tug at the roots of established thinking, then, to read of the above account by the French authors and learn that not only a complete hypophysectomy was carried out but that the patient was alive and well eight months later with definite improvement in the exophthalmos. Although signs of pituitary insufficiency developed postoperatively, the patient was carried along reasonably well on a regime of 15 mg. of cortisone, 2 cgm. of thyroid extract, and 10 units of posterior pituitary powder.

The patient that the French authors described seemed to be in a rather severe predicament (severe hyperophthalmopathy, marked proptosis with exposure keratitis, secondary glaucoma, and central scotomas) and the authors proceeded with hypophysectomy only after all other accepted methods of treatment had failed to arrest the progress of the disorder. These authors felt that in the severe situation of this patient something more than palliative (i.e. orbital decompression) treatment should be attempted.

Because of recent advances in hormone chemistry, it is now possible to offer substitution therapy in the form of various "synthetics" and "biologicals" for many endocrine deficiencies. By such substitution therapy patients who have undergone either adrenalectomy or hypophysectomy for malignancies are being maintained. It is not unreasonable to assume, therefore, that in selected cases undergoing hypophysectomy for malignant exophthalmos in the future a reasonable balance of the metabolic bookkeeping can be maintained during the postoperative period. Although I have corresponded with several medical centers where the surgeons are doing hypophysectomies for various disorders, I have not found any instance wherein this operation has been attempted for malignant exophthalmos in the United States.

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SURGERY OF UNILATERAL EXOPHTHALMOS

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Acta XVII Councilium Ophth., 1954, 599–608

A surgical intervention is necessary in the treatment of unilateral exophthalmos caused by an orbital tumor when there is exposure of the cornea and keratitis

that may cause loss of the eye or when alterations of vision appear as a result of (1) pressure or involvement of the optic nerve or (2) marked intraorbital hypertension. In performing the operation the transfrontal approach is the procedure of choice in most cases. It permits a good visualization of the orbital structures during the exploration of the orbital cavity, which is carried out following the scheme of Charpy's anatomic spaces of the orbit. The transfrontal approach should be used in the removal of meningiomas of the lesser wing of the sphenoid that are causing unilateral exophthalmos and also in the removal of tumors that are located behind the globe of the eye. It should not be used when unilateral exophthalmos seems to be the result of orbital cellulitis. In cases of malignant tumors evisceration of the orbit is definitely indicated. Anterior tumors, when large in size, are approached by lateral orbitotomy (Kroenlein). If they are not large, they can be approached by any of the various methods of orbitotomy. Tumors that are located in the floor of the orbit are rare. They can be approached by the transmaxillary route. Osteomas that originate in the ethmoidal sinuses can be removed by the transfrontal approach provided precautions are taken to prevent infection.

The intraorbital stages for exploration of the orbital cavity, with findings related to Charpy's anatomic spaces of the orbit, are as follows: The periosteum is separated from the bone. This separation offers no difficulty. The intraorbital structures which occupy the peripheral space can be visualized in this space, through the more or less transparent periosteum. The lacrimal and supraorbital nerves are seen in an area outside of the space, before they meet at the orbital apex to form the ophthalmic nerve. The trochlear nerve is seen in the space a little below the lacrimal and supraorbital nerves. Blood vessels branching off from deeply located ones are visible in the most anterior part of the orbit. The ophthalmic nerve is seen after the point at which the lacrimal nerve branches off. It passes forward over the levator palpebrae superioris and the rectus superior muscle and forms an angle with the mass of these muscles. In an inner area of the space the trochlear nerve is seen, when it passes over the levator palpebrae superioris near the point of its insertion into the orbital apex. The periosteum is sectioned anteroposteriorly in order to prevent injury to the intraorbital structures located in the peripheral space. The section is made along the external border of the muscular mass (formed by the levator palpebrae superioris and the rectus superior muscle seen earlier through the periorbit) or along the external border of the supraorbital nerve in a direction that is parallel to the main axis of the orbit.

In the peripheral space the muscular masses of the levator palpebrae superioris and of the rectus superior are identified within the space and those of the external rectus muscle are identified without the space. The intermuscular membrane that binds these muscles is thick anteriorly and thin posteriorly. This membrane is sectioned in a direction that is parallel to the external border of the levator palpebrae superioris. After this membrane is sectioned, the muscular conus (central space) is entered. In this are located the main nerves and blood vessels of the orbit. Ample visualization of the structures located in this space can be

obtained by moving inwardly the levator palpebrae superioris and the superior rectus muscle. It is not necessary therefore to section the transversal muscles to obtain a good visualization. Care should be taken during all the maneuvers performed in the exploration of the orbital cavity to prevent injury to the superior division of the oculomotor nerve which supplies the superior rectus muscle and the levator palpebrae superioris. The oculomotor nerve approaches these muscles from its deep aspect at the level of the posterior third of the orbit. In a similar way the trochlear nerve approaches its muscle from its internal aspect in the posterior third of the orbit. Visualization of the structures that are deeply located in the orbit is difficult. To continue the exploration the surgeon resorts to palpation of the structures. The optic nerve is thus identified as if it were a hard cord and the globe of the eye is identified in the anterior part of the orbit.

In cases in which the presence of round tumors is suspected the anesthetist is requested by the surgeon to exert pressure on the eye, over the eyelids, so as to identify the globe of the eye through the transmission of its movement during the pressure. The optic nerve is surrounded by nerves and blood vessels that are greatly important to the ocular functions. Therefore, extreme precaution should be taken with regard to these structures during the maneuvers performed in exploring the orbit. In cases in which there is a tumor about the optic nerve which is suspected of being malignant, section of the optic nerve with complete removal of all the areas suspected of being malignant is definitely indicated.

In the exploration of, and approach to, tumors that are located below the optic nerve, it must be kept in mind that the ophthalmic artery, the superior ophthalmic vein, and the nasociliary nerve follow a forward trajectory, first outside of the optic nerve and then passing over the nerve. It is at this point that these structures give off the most important vascular and nervous branches to the eye. The ciliary ganglion is located on the external aspect of the optic nerve at the level of the posterior third of the orbit. The nerves arriving at and leaving this ganglion are located outside of and above the optic nerve. Tumors that are located in zones situated below the optic nerve are approached from the internal side of this nerve, after the levator palpebrae superioris and the rectus superior muscle have been displaced inwardly. Great care should be taken to prevent injury to the nerves which supply these muscles as well as to that which supplies the internal rectus muscle. This nerve branches off from the lower branch of the oculomotor nerve at the level of the external aspect of the optic nerve. It passes under the optic nerve and advances inwardly to reach its muscle in its middle third. In nine patients with unilateral exophthalmos owing to orbital tumors, these were removed by a surgical intervention. The tumors were meningioma of the wing of the sphenoid in three instances, and fibroma, cavernous angioma, cystic astrocytoma, chronic inflammation of the orbit, reticulosarcoma, and neurofibroma in one case, each. No operative mortality occurred in this series of patients.

Comment: In this article the authors review the ophthalmologic, neurosurgic, and neuroradiologic aspects of unilateral exophthalmos. The authors emphasize the need for correct clinical evaluation of any possible tumor, pseudotumor, or ophthalmoplegic

exophthalmos that may occur within the orbit so that the correct approach to treatment may be determined. The radiographic findings, the methods of diagnostic angiography, and the important anatomical features relating to this subject are reviewed. The authors detail their experiences with nine orbital tumors (three meningiomas of the sphenoidal wing, one fibroma, one cavernous angioma, one cystic astrocytoma, one chronic inflammatory pseudotumor, one reticulosarcoma, and one neurofibroma). Those who read Spanish easily would be interested in reviewing the complete paper. Only the section dealing with the "surgical considerations" has been condensed above.

In their surgical approach to cases of unilateral exophthalmos the authors obviously favor the transfrontal approach chiefly on the basis of the good visualization that it provides. Their statements, however, are quickly qualified by further pointing out that lesions along the floor of the orbit can be approached by the transmaxillary route, neoplasms in the ethmoid sinuses can be removed by the transfrontal route providing precautions are taken to prevent infection, and that anterior tumors can be approached by the lateral route. By reason of these qualifying statements their arguments for the use of the transfrontal approach seemed a little less convincing to this reader.

I am in quite hearty agreement with the authors that whenever there is visual impairment due to interference with the function of the optic nerve, or radiographic evidence of erosion or sclerosis along the optic foramen or wings of the sphenoid bone that a transfrontal procedure should be given first consideration in the approach to the involved orbit. If these definite signs of trouble in the posterior orbit are absent, however, my enthusiasm for the transfrontal approach wanes in favor of the lateral approach which, I believe, offers about as much visual advantage as does the transfrontal approach but with less trauma and danger to the patient.

As concerns the removal of tumors in the region of the ethmoid sinus, I think any consideration of the transfrontal approach is unnecessary. Most qualified otorhinologists are able to remove the majority of these lesions through an intranasal route. If there is any question of obtaining a better field of exposure for the removal of such lesions, the so-called "lateral rhinotomy" may be performed. Some otorhinologists even prefer the frontoethmoid approach wherein they skim along the medial wall of the orbit to reach the offending sinus. In all of these approaches the chances of harmful postoperative infection are practically nil as compared to the transfrontal approach.

It is fortunate that tumors in the lower posterior nasal quadrant of the orbit are less frequent than in any other area of the orbit, for this is a veritable "no man's land" so far as surgical accessibility is concerned. There has not been a suitable approach yet invented for this region. The distances involved from the point of entry into the orbit toward the area in question are about equal whether the transfrontal or the lateral approach is utilized. If the lateral approach is performed, the lateral rectus muscle must be lifted to gain access to the lower nasal quadrant. If the transfrontal approach is performed, the muscle insertions of the superior rectus and levator palpebraris must be moved to one side. Since it is easier to manipulate the lateral rectus than the combined muscle bellies of the superior rectus and levator muscle, I would favor the lateral approach over the transfrontal approach if the choice lay between these two routes.

The authors give a detailed description of the various stages of their intraorbital procedure. As I read this description I can readily visualize the various orbital structures as they pass from one surgical plane to another.

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THE PUPIL

THE NORMAL PUPIL AND THE ARGYLL-ROBERTSON PUPIL IN CONVULSIVE SEIZURES

J. Gottschick

Arch. f. Psychiat. u. Nervenkrank. 1955, *193:* 117–130

The present-day knowledge of the behavior of the pupils during cerebral-organic convulsive seizures is insufficient and the literature contradictory. It is, therefore, not an adequate aid in differential diagnosis. The pupillary behavior of patients subjected to electric shock treatments consists of three phases.

A. *Normal Pupil:* (1) Slightly preceding, or simultaneous with, the onset of convulsive seizures the pupil dilates, for example from an initial diameter of 3.5 mm. to 7 mm.; during this time both the light reflex and dilation in response to sensory stimuli are abolished. (2) During the post-convulsive comatose stage the pupil is mitic and fails to respond to light and to sensory stimuli. (3) In the delirious and following somnolent phases, rapid spontaneous oscillations of pupillary dilation and constriction appear; the light reflex returns and vigorous dilation is elicited by painful stimuli.

The pupillary behavior during the first (tonic-clonic) and the third (post-convulsive delirious and somnolent) stages is difficult to distinguish from similar phenomena in hysterical or simulated convulsive attacks. In contrast, the miosis with loss of reactivity during the post-convulsive comatose stage is characteristic of organic seizures and is otherwise found only in deep narcosis or in coma. The outstanding characteristic of pupillary behavior in true organic seizures is, therefore, the miotic stage.

B. *Argyll-Robertson pupil:* Four cases are presented. Essentially the same sequence of pupillary motions as described above occurs, but they are mostly reduced and sluggish. They measure no more than 1–1.5 mm. in the complete Argyll-Robertson syndrome (with intense miosis and complete absence of the light reflex) and are slight and sluggish in incomplete cases. The pupils of these patients dilate 2–3 mm. under the influence of atropine. After local administration of atropine or of adrenaline the dilation due to the shock treatment appeared to be enhanced. Pupillary dilation to pain stimuli was poor or absent.

The characteristics of the Argyll-Robertson pupil are listed as follows: (a) Changes in the iris; (b) absent dilation to cocaine; (c) slow and incomplete dilation to atropine; (d) no dilation to instilled adrenaline; (e) marked miosis; (f) loss of light reflex; (g) loss of dilation to pain stimuli; (h) good or even exaggerated contraction to near vision; (i) presence of the "lidclose" reflex, i.e., pupillary contraction upon forced closing of the eyelids. These points are discussed with particular reference to the opposing theories of Merritt and Moore (The Argyll-Robertson pupil. Arch. Neurol. & Psychiat., *30:* 357) on the one

hand and of Poos on the other (Das System der Pupillenstarre in seinen kausal-genetischen Zusammenhängen. Arch. f. Psychiat. u. Z. Neur., *183:* 493). Merritt and Moore assume a central nervous lesion involving the last afferent neuron of the light reflex arc between pretectal area and third nerve nucleus and also the descending pupillary dilator fibers from the hypothalamus. Poos assumes a peripheral condition in the iris itself, whereby primarily the neuro-muscular transmission is disturbed while the muscles themselves are less damaged.

It is concluded that neither of these theories covers all of the findings listed above and that two separate lesions have to be assumed, namely (1) a central nervous interruption of the light reflex arc, probably between the pretectal area and the third nerve nucleus and (2) damage to the iris dilator muscle or its sympathetic neuro-muscular transmission. This unsatisfactory state of affairs calls for accumulation of more data, and the pupillary phenomena occurring during electrically induced convulsive seizures appear particularly suitable.

Comment: The attempt to analyze the Argyll-Robertson syndrome from the pupillary behavior during epileptic seizures is, as far as we know, new and original with the author. Unfortunately, the physiological and particularly the pupillary phenomena occurring during electrically induced convulsive seizures are complex and their mechanism is at least as unknown as the mechanism underlying the Argyll-Robertson phenomenon. Accurate observation of the pupils with the unaided eye, most difficult even when under ideal conditions, becomes almost impossible during convulsions in which head- and eye-movements participate. The interaction of various factors, both sympathetic and parasympathetic, excitatory and inhibitory, which participate in the pupillary reactions during convulsive seizures are still too obscure to serve as a basis for the explanation of other pupillary phenomena. Therefore the author's suggestion, interesting as it is, represents, at least at present, an attempt to explain an unknown phenomenon by observations concerning a second unknown phenomenon.

The characteristics of the Argyll-Robertson pupil enumerated by the author are accepted by a large number of workers. Pupillographic analysis convinced us, however, that some of them are erroneous. (Lowenstein, O.: Miosis in the Argyll-Robertson syndrome and related pupillary disturbances. A. M. A. Arch. Ophth. In press.)

(1) Pupillary dilation to instilled cocaine is often not at all disturbed in patients showing the Argyll-Robertson syndrome. We found it delayed and inextensive, but not absent, in late cases with obvious iris damage, where reactions to all physiological stimuli and to other autonomic drugs were also impaired.

(2) The dilation to atropine of the Argyll-Robertson pupil is not less than normal. It should be stressed that the normal pupil dilates no more than 1 to 2 mm. when atropine is instilled in darkness. When the test is done in light, the abolition of the light reflex of the normal pupil makes the dilation to atropine appear greater than it actually is. It is true that many (not all) Argyll-Robertson pupils fail to reach as large a diameter after atropine as the normal pupil. These cases usually show iris damage and react poorly to all stimuli.

(3) Dilation to painful stimuli is rarely abolished in Argyll-Robertson pupils, although it is frequently less extensive than that of the normal pupil. The reduction is, however, not more than would be expected in the presence of an increased sphincter tone. When eserine is instilled, the normal pupil shows similar reduction in reflex dilation.

(4) The author states that the marked miosis seen in Argyll-Robertson pupils can be

explained by weakness of the pupillary dilator mechanism, as is seen in Horner's syndrome. But in complete Horner's syndrome (uncomplicated by other pathology) the pupil is no smaller than about 5–6 mm. in darkness, while Argyll-Robertson pupils may be as small as 1 mm. Such small pupils cannot be explained except on the basis of increased sphincter action. The dilation to atropine (in the absence of light reflexes) proves the cholinergic nature of the miosis.

In spite of these negative comments, the importance of this conscientious work should not be underestimated. Its careful observations and thoughtful comment make interesting reading and may be the basis of fruitful future research.

OTTO LOWENSTEIN

THE RETINA AND VITREOUS

CONTRIBUTION TO PATHOLOGY OF HEMORRHAGES INTO THE VITREOUS BODY

F. GRAUPNER

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Zentralbl. ges. Ophthal., 1955, *65:* 323

Cases of vitreous hemorrhages are reported in which careful examination of the periphery of the eye showed that the bleeding was caused by tears of the retina. In none of these cases were the tears associated with detachment of the retina. The tears were not situated in the extreme periphery, but in the centre between the equator and the periphery, so that the retina always remained visible peripherally from the tear. In all cases, there was marked cystoid degeneration, gray-white discoloration, migration of pigment and obliteration of small vessels.

Formation of cysts in this part of the retina is a phenomenon which may be observed frequently, and clinical findings make it probable that the tears of the retina are tears in the inner wall of the cysts. The outer, near to the choroid, is still unimpaired and prevents the communication with the retroretinal space. The bleeding originates in the torn inner wall of the cyst in which the retinal vessels are situated which frequently are partially obliterated.

One case was particularly illustrative in that the tear remained unchanged for 18 months and then suddenly was followed by an extensive detachment of the retina. The original tear was surrounded by the adjacent retina. Choroidal changes or accumulations of pigment were not observed, but the sudden onset of the detachment suggested that the posterior wall was torn and that fluid got behind the retina. In this case, the patient refused surgical intervention at the time of the first tear. The fact that a very unfavorable detachment of the retina may result from a tear of the retina makes the problem of surgical intervention an important one. Such tears of the retina should be closed on principle, and larger, floating tears must be coagulated at once in an attempt to prevent further tears. In cases of small tears which remain stationary, and in which lightening phenomena subside, one may practice expectant treatment with vasodilating drugs. Electrocoagulation through the sclera may be considered a major surgical intervention as compared with the size of the tear, and it also may be difficult to get the patient's permission for it. In cases similar to those reported by the author, satisfactory results may be obtained by light-coagulation of the retina through the inner eye according to Meyer-Schwickerath's technique. Closure of the tear by coagulation of the adjacent area is recommended to prevent a tear in the posterior wall. In an attempt to localize the area of the tear, the periphery of the eye should be checked carefully in case of every bleeding into the vitreous body, of more extensive vitreous hemorrhage, and of lightening phenomena.

Comment: Our knowledge of the pathogenesis and of the fate of macular cysts exceeds that of retinal cysts in a more peripheral location. While rupture of the outer wall of a macular cyst leaves a permanent central scotoma, rupture of its inner wall is not associated with either subjective or objective phenomena unless its content was turbid, in which case the vision is improved by the rupture.

Not so with peripheral cysts. There, rupture of the inner wall severs a vascular layer. It is surprising that this etiology of vitreal hemorrhages has not been emphasized before.

It is probably significant that the author finds these partial tears which have led to vitreous hemorrhages not in the extreme periphery but just beyond the equator, where the capillary layers are still well developed, and where, in extensive posterior vitreal detachments, the dividing line between detached and undetached vitreous frequently lies.

Since the splitting of the retina in cystic degeneration usually occurs along the outer molecular layer, leaving a thin outer and a thicker inner wall, some additional factor must be present to precipitate rupture of the thicker wall. This may be a membrane on the inner retinal surface, such as forms in places where the vitreous and retina have lost contact over a period of time, or it may be an unusually firm vitreo-retinal adhesion.

At any rate, pathological changes in the vitreous appear to be a prerequisite for inner ruptures of peripheral retinal cysts such as the author describes and it is too bad that he does not mention the appearance of the vitreous in his cases.

It is interesting in view of another recent publication on retinal holes (Michaelson, Acta XVII Councilium Ophth., 1954, 392) that the author found small, obliterated retinal vessels and pigment migration into the retina adjacent to such partial retinal tears, suggesting an etiologic entity similar to that described by Michaelson.

BERTHA A. KLIEN

RETINAL DETACHMENT: CLINICAL EVIDENCE OF THE ROLE OF THE CHOROID

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Acta XVII Councilium Ophth., 1954, 392–403

Evidence indicates that choroidal disturbance with atrophy of the choriocapillaris, cystic degeneration of the retina, and a retinal hole form a chain of events in certain cases of retinal detachment. Although the intermediate link, cystic degeneration of the retina, cannot usually be detected clinically, especially if it is local in nature, it might have been supposed that the association of the first and third, i.e., choroidal disturbance and a retinal hole, would often have been described in clinical reports. In fact, however, very few such reports have been made.

Recent studies of 10 eyes revealed the existence of 15 foci at which this association was present, either actually or potentially: all showed a characteristic

syndrome of a pigmented choriodopathy, sclerosis with or without occlusion of the local retinal vein, retinal hole formation, and usually retinal detachment, with these elements appearing in the order given. The focus was situated in the majority of cases about 5 mm. from the ora serrata. At three foci, a retinal hole was not observed, but these foci obviously belonged to the others because of the presence of similar foci with holes or retinal detachment in the same or the fellow eye. The choroidopathy was invariably pigmented, flat, and limited in extent. Neither white exudative choroiditis nor choroidal atrophy with scleral exposure was observed at these foci. The venous sclerosis had the same character in each case, with parallel sheathing of the larger vein and fine white lines representing sclerosis of the post-capillary venules, all together sometimes creating a fish-bone appearance. The presence in the neighborhood of the sclerosed vein of small rounded hemorrhages is characteristic of partial occlusion of the vessel.

The retinal hole was usually circular; when oval, its axis was aligned with the direction of the local vein. Interestingly enough, if two or three holes were present, they too were aligned with the direction of the local vein.

Apparently, the choroidopathy is capable of producing a phlebosclerosis in the overlying retinal vein and the fine post-capillary venules. It is not unusual for a choroiditis to cause phlebitis of the local retinal vein. It was noted that if the sclerosis affects the post-capillary vessels at one side of the vein only, it is usually on the side next to the choroidal patch. The retinal hole appears after the choroidopathy and the phlebosclerosis. Since the choriocapillaris nourishes the outer portion of the retina and the retinal vessels nourish the inner portion, the conditions necessary for a local loss of nutrition affecting the entire thickness of the retina are obviously present. The resulting retinal dissolution as represented by a hole may be seen, while the intermediate microscopic phase, the cystic degeneration, may be inferred. The syndrome is not uncommon, having been found in about 20 per cent of all eyes suffering from retinal detachment observed during the year 1953.

Comment: The interesting triad of findings, viz., pigment migration into the retina, localized retinal phlebosclerosis and adjacent retinal hole formation, which the author describes, seems to constitute an etiologic entity in a certain type of retinal detachment.

The author refers to the pigmentary disturbance as choriopathy and believes the sequence of events to be: choriopathy, retinal phlebosclerosis, retinal hole formation. No other signs of a pathologic process in the choroid such as atrophy, visibility of choroidal vessels, or exposed sclera were present in his cases.

To explain the pigment migration into the retina, no choroidal process has to be assumed. It is much more probable that the primary lesion is the retinal phlebosclerosis with varying degrees of occlusive phenomena, leading to low grade chronic edematous imbibition of the surrounding retina, destruction of some retinal elements and reactive proliferation of pigment epithelium, which is irritated by some of the edematous fluid reaching its inner surface. Cystic degeneration of the retina would be a natural consequence of such pathologic processes.

This triad of findings may exist for varying periods without retinal separation (18 months in one of Graupner's cases), but prophylactic surgery should be considered early.

BERTHA A. KLIEN

HEREDITARY DISEASE

INTERMEDIARY INHERITANCE OF RECESSIVE-SEX-LINKED DISEASE

B. Fleischer

Deutsch. Ophth. Gesellsch., 1953, *57:* 261–264

In a lecture presented in 1920 the author stated that according to his experience mothers, daughters, and other female descendents of color-blind men, not rarely show mild weakness of the color sense. This partial dominance of the pathological gene over the normal in transmitters is illustrated by a case of chorioideremia in its last stage in a 49-year-old man and chorioretinal changes in his daughters. In the man there was almost complete absence of the choroid with a few remainders in the periphery, capillary redness of macula and papilla, ring-shaped conus around the papilla, with a myopia of 5.5 diopters, isolated black pigmentary foci on the exposed sclera, and fine, snuff-like pigment at the periphery, several larger trunks of vortex veins, and central remainders of visual field.

This anomaly is a recessive-sex-linked hereditary degeneration of retina-choroid; it is not a congenital absence of the choroid, but a progressive disorder in the course of which atrophy of the choroid occurs gradually. Reports by other workers showed highly characteristic changes of the fundus oculi in female transmitters who did not present subjective symptoms; these changes consisted of changes of the retinal pigment, particularly at the periphery, pepper- and salt-like and partially arranged in radial order, but not typical retinitis pigmentosa. The changes were not progressive.

Because of these reports, four sons and two daughters of the patient were examined. Findings in the sons were completely normal. The two daughters, aged 17 and 5½ years, were healthy, did not have any subjective symptoms of a visual disturbance but had peripheral chorioretinal degeneration of the pepper and salt pigmentary type, with normal visual acuity and normal light sense. This suggests the practical significance of recognizing the transmitter qualities with regard to eugenic procedures in case of pernicious disease which may lead to blindness. The theoretic importance of this observation is of similar magnitude.

There are additional recessive-sex-linked diseases of the eye, and their manifestation in heterozygous women seems likely. This was confirmed by a case of retinitis pigmentosa associated with myopia and by the stationary congenital hemeralopia associated with myopia. Other illustrative cases were collected from the literature, including cases of hereditary nystagmus and of albinism of the eyes.

Comment: Dr. Fleischer has most ably discussed the more well known sex-linked intermediate diseases of man. Most of these display ophthalmological signs or symptoms which are of interest in our discipline. The knowledge of the existence of, and the ability

to recognize the carrier-state of such diseases provides the ophthalmologist with excellent diagnostic as well as prognostic advantages.

The difficult ophthalmoscopic diagnosis of early or late choroideremia, ocular albinism, retinitis pigmentosa is clarified if one takes the trouble to study, when available, the retina of the affected patient's mother or daughter. The examiner is immediately able to prognosticate accurately that none of the male offspring of an affected male will be afflicted (excluding consanguinous matings) and that all of the daughters will be carriers and will exhibit the typical ophthalmoscopic "carrier state." This carrier female will transmit the deleterious gene to 50 per cent of her female and to 50 per cent of her male offspring. The male, having no counteracting normal gene to ameliorate the effect of the x-borne gene, will exhibit the serious form of the disease. The carrier daughters however do have another paired and normal gene so that they merely exhibit the very mild yet clinically detectable state.

The terms recessive and dominance are merely relative and it is becoming increasingly evident that most "hidden" genes exhibit some sign of their presence. Dr. Fleischer, in this vein, points out that female carriers of such genes producing megalocornea, albinism, hemophilia, Pelizaeus-Merzbacher's disease, congenital stationary night blindness, Leber's disease, color anomalies, and so forth may not infrequently exhibit the clinical presence of the disease.

HAROLD F. FALLS

SEVERE MALFORMATIONS OF EYES IN PATIENTS WITH ULLRICH'S SYNDROME OF DYSCRANIO-PYGO-PHALANGY

G. MEYER-SCHWICKERATH

Deutsch. Ophth. Gesellsch., 1953, *57:* 147–150

A case of Ullrich's syndrome of dyscranio-pygo-phalangy is described in a weak baby boy who was born at term and had a birth weight of 2620 gm. (five and a half pounds). Both parents were normal and not related to one another. The infant had brachycephalia and acrocephalia. Roentgen ray examination of the cranium revealed a skull with definite congenital gaps in the bone, with wide-open cranial sutures and a frontal encephalocele, which covered the projecting forehead. Facial lines were coarse, the broad root of the nose was sunken. The ears were underdeveloped. There was a spina bifida aperta in the lumbar region. All four extremities showed hexadactylism; the sixth member of the otherwise normal extremity formed a small ulnar appendage without bony connection.

On the second day of life the eyes were examined and the findings were as follows: The small, adequately movable eyeballs were situated deep in the orbits. The corneal diameter measured 7 mm. on the right and 5 mm. on the left. The corneal parenchyma in both eyes symmetrically showed a fine diffuse opacity in the nasal lower quadrant. The anterior chamber was very flat in both eyes. The

atrophic iris was of dirty-brown color. The pupil was very wide and showed on the right side a notch at 3 o'clock, and at the left side two notches at 9 and 7 o'clock. The lenses did not show visible opacities in the anterior and median layers. Immediately on the posterior surface of the lens a yellowish tissue was visible at both sides, through which many vessels were passing.

The child died six days after birth and autopsy was performed immediately. The right eye was 12 mm. long and 11 mm. in height and width. In the left eye, the length, width and height were 9 mm. Microscopic examination of the eyeballs revealed the same changes in both eyes, which however were less pronounced in the left. The globe appeared well-proportioned except for the relatively considerable thickness of the coats of the eye, which corresponded with that of a normal newborn infant. The iris showed an incomplete aniridia with the development of only short stumps. Sparse muscle fibers could be demonstrated in several areas. The pigmentary leaf of the iris showed a hollow space between the two pigmentary layers, which was considered to be the remainder of the optic vesicle. The hypoplastic ciliary body did not show any ciliary processes, except for a small area at 7 o'clock, where it was reached by the retinal tissue. The lens showed an extensive homogenization by the fibers at the posterior pole. The epithelium had proliferated to the dorsal surface around the equator and here was connected directly with a tissue plate, which consisted of displaced layers of the retina and the pigmentary epithelium and some undifferentiated embryonal tissue. In this tissue many vessels and faintly pigmented cells were visible. In the nasal area retrolental tissue plate continued downward with a band of tissue consisting of retinal elements showing numerous rosettes. The retina was well developed in the temporal half of the globe. The optic nerve, surrounded by a mantle of primary ectodermal cells, showed good development of the nuclear column in its anterior portion. At the nasal, inferior edge of the optic nerve the nervous fibers projected considerably into the interior of the bulbus.

Thus a microphthalmic globe with an incomplete aniridia was found. The retina showed defective development and displacement and was forming a retrolental plate together with undifferentiated tissue. The optic nerve showed a circumscribed displacement into the interior of the bulbus, with a persistence of the primary papilla and of the hyaloid artery. This change in the papilla combined with the displacement of the other portions of the primary optic cup seems to be of particular significance. It is suggested that hereditary and environmental factors may have cooperated in the production of the malformation in the reported case.

Comment: Dr. Meyer-Schwickerath's plea for publication of well-studied cases of syndromes which include involvement of the cranial structures deserves the support of ophthalmology. It will be only through many such thorough studies as this that we will eventually learn what is necessary concerning their etiology. Noxious intrauterine agents acting at a specific time interval in organogenesis may effect changes undetectable clinically (phenocopies) from those known to be affected by gene action. It thus behooves the ophthalmologist to be thoroughly acquainted with the maternal health during the specific pregnancy as well as with that family's pedigree. It is correctly pointed out, moreover, that both environmental and gene influences may require certain gene milieu through

which to produce a given response. The author concludes, since he is unable to present evidence for either abnormal heredity or noxious environmental agent in his case, that the end product is most likely a combination of the effects of both nature and nurture. The possibility of mutation as a causative agent was not considered but should always be kept in mind when one is confronted with such sporadic cases of developmental aberration.

HAROLD F. FALLS

THE PRODUCTION OF TEARS IN FAMILIAL DYSAUTONOMIA PRELIMINARY REPORT

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J. Pediat., 1956, *48:* 328–329

Familial dysautonomia, which was first described in 1949 by Riley and associates, is characterized by excessive perspiration, drooling, cold skin, erythematous skin blotches with excitement, emotional instability, hypertension, postural hypotension, and inadequate temperature control. In addition, poor motor coordination, absent or diminished deep tendon and corneal reflexes, and relative indifference to pain suggest a more diffuse involvement of the central nervous system. Defective lacrimation with absence of visible tears has been a characteristic diagnostic feature of the disease. Corneal ulceration has frequently resulted from the deficient tearing and corneal hypalgesia.

An unexpected but apparently significant finding was obtained when acetyl beta-methyl choline (Mecholyl) was injected subcutaneously as a test for pheochromocytoma in a patient with familial dysautonomia and paroxysmal hypertension. Mecholyl failed to stimulate a significant rise in blood pressure, but surprisingly caused the formation of visible tears. This chance observation prompted further study of the induction of lacrimation by Mecholyl in two other patients with familial dysautonomia. In all three of these patients, who were aged 2, 6, and 14 years, respectively, Mecholyl, by subcutaneous injection in a dose of 3 mg. for the children and 5 mg. for the adolescent, produced drops of tears which rolled down the inner canthus. This dose of Mecholyl was the same as that required to produce tears in normal controls. Neostigmine methylsulfate (Prostigmin) 0.25 mg. subcutaneously was also effective. All previous attempts to produce tears had failed, and the patients had shown an obtunded reaction to various unpleasantly irritating odors.

The observations in these cases indicate that Mecholyl, neostigmine, and other parasympathomimetic drugs may prove useful in the prevention and treatment of corneal ulceration in patients with familial dysautonomia. They also show that

the lacrimal gland in this condition can function as a normal end-organ when stimulated directly by such drugs. The defect in lacrimation in this disease must therefore depend on an abnormality in the nerve pathways. The appreciation and effects of stimuli over the sensory afferent and central receptive pathways are distinctly defective in the three patients studied. It is not known whether there are additional defects in the central nuclei for psychic crying, and in the chemical transmission of impulses at the synapses of the parasympathetic efferent pathway.

SYSTEMIC DISEASE

CENTRAL RETINAL VEIN OCCLUSION IN JUVENILE DIABETICS; CASE REPORT WITH CONSIDERATION OF THE PATHOGENIC RELATIONSHIP BETWEEN DIABETIC RETINOPATHY AND RETINAL VEIN OCCLUSION

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Occlusion of the central retinal vein is a tragic condition because in about 75 per cent of the cases it leads to sudden and lasting blindness in the affected eye. Central retinal vein occlusion occurs most often in the old age groups and is generally accepted as being related to diabetes, hypertension, and other diseases characterized by extensive vascular lesions. The coexistence of central retinal vein occlusion and diabetes in younger patients has not previously been reported, although increasing longevity has made juvenile diabetics (those in whom the onset of diabetes occurred at 15 years of age or under) particularly subject to vascular degeneration.

This report deals with central retinal vein occlusion found in three young male diabetics (ages 15, 25, and 37 years; duration of diabetes, 12, 18, and 26 years, respectively), and in one young female diabetic during pregnancy (age 22 years, duration of diabetes, 11 years) within a period of only six months. The general use of the collective terms, retinal "arteries" and retinal "veins" is misleading, inasmuch as these vessels are arterioles and venules by histologic definition and behave as such by pathophysiologic response. Realization of this latter fact in particular, together with the results obtained in the authors' *in vivo* investigations of the microscopic reactions of the small vessels of the bulbar conjunctiva in young diabetics, strongly suggests that the characteristic venous retinal changes and their underlying cause in young diabetics should be reinterpreted. The reinterpretation, when made, seems to show a clear pathogenic relationship between the development of diabetic retinopathy and retinal vein occlusion in these young patients.

The existence of such a relationship was borne out by the concomitant development in one of the authors' patients—a 15-year-old boy—of diabetic retinopathy in one eye and central retinal vein occlusion in the other. The occurrence of both conditions in immediate time-relationship in this patient, the youngest in whom central retinal vein occlusion has apparently been reported, afforded an unusual opportunity for the detailed observation of the vascular reactions and the morphological changes in two different tissues, the retina and the bulbar conjunctiva (representing the subcutaneous tissue) simultaneously, both at the time of the lesion and subsequently at a three-year follow-up.

The retinal changes in young diabetics consist chiefly of venous distention, microaneurysms, and the proliferation of new vessels. Although diabetic retinopathy and central retinal vein occlusion are two distinct clinical entities, they have many ophthalmoscopic features in common, and on pathoanatomic study the similarities between them are even more striking. Capillary microaneurysms, which are the characteristic lesion in diabetic retinopathy, have also been repeatedly demonstrated in central retinal vein occlusion; in addition, both conditions are characterized by a distortion of the capillary network, new formation of vessels, and dilated venules with evidence of fatty degeneration. Microaneurysm formation in central retinal vein occlusion is apparently due to the sudden occurrence of stasis which causes anoxia and undernutrition of the venular and capillary walls leading to focal mural degenerative changes of the basement membranes and aneurysm formation. Since the production of capillary microaneurysms in diabetes may be similarly explained, it appears that stasis in the venous circulation is the common pathogenic factor in both diabetic retinopathy and retinal vein occlusion in young diabetics.

Comment: Diabetic retinopathy and retinal vein occlusion are each characterized by capillary aneurysms, hemorrhages in the retina and vitreous, retinitis proliferans, rubeosis iridis, and hemorrhagic glaucoma. Furthermore, there is an increased incidence of vein occlusion in patients with diabetic retinopathy. On the basis of these relationships, there has been repeated speculation about the role of venous obstruction or stasis in the pathogenesis of diabetic retinopathy. This is an attractive hypothesis, but one must remember diabetic retinopathy is often seen without clinical or pathologic evidence of atherosclerotic changes, venous occlusion or venous obstruction. Furthermore, vein occlusions occur in the absence of diabetes and can be induced experimentally in non-diabetic cats or rabbits. The capillary aneurysms associated with this obstructive disease process can usually be differentiated in appearance and location from those seen in diabetic retinopathy.

The hypothesis that capillary aneurysms are a result of a metabolic derangement of the retinal capillary cannot be refuted. Although retinal capillary aneurysms result from local obstruction or inflammation, the existence or role of stasis in the formation of the other varieties of capillary aneurysms remains unproved. Further elucidation is nedeed of the metabolic alterations in the retinal capillary associated with long-standing diabetes or following the administration of adrenocortical hormones.

BERNARD BECKER

OCULAR MANIFESTATIONS OF KAPOSI'S VARICELLIFORM ERUPTION. DISSEMINATED CUTANEOUS HERPES SIMPLEX

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Rivista Oto-Neuro-Oftal., 1955, *30:* 519–550

A case of Kaposi's varicelliform eruption involving the eyes is described in an 8-month-old infant in whom exudative eczema of the face had developed when he was 4 months old. Four days before admission to the clinic, high fever developed and small vesicles appeared on the involved skin of the face. On admission, fever was high and numerous pustular-umbilicated vesicles were present on the face, scalp, and tongue. The eyelids were partly involved by the eruption and the conjunctivae were slightly reddened, without secretion. A slight hepatosplenomegaly was present. The child had not been vaccinated recently nor had he had contact with persons who had been vaccinated recently or had varicella. His general condition was grave, the vesico-pustular eruption spread to other parts of the body, and, on the 6th hospital day, frank encephalitic symptoms appeared which lasted about 3 weeks.

On the 13th hospital day, the conjunctivae became markedly red and the beginning of a corneal ulcerative process was observed in both eyes; it was more pronounced, however, in the right eye. By night, the lesions had assumed the aspect of a dendritic keratitis that was characterized by bilateral centrocorneal figures of fine arborization, with an extremely mild iridal reaction. The following day, the dendritic aspect of the lesion was still present in the right eye, whereas the left eye showed an extensive corneal ulceration that involved also the most superficial layers of the parenchyma. Marked bilateral corneal hypoesthesia was present. Four days after the onset of the keratitis, the corneal necrosis, having extended to the deeper layers of the parenchyma, caused the onset of a marked descemetocele in the left eye, while the lesions in the right eye tended to become deeper and converge, thus assuming the aspect of a central disk-like infiltrating process. Corneal anesthesia was now present bilaterally, and cutaneous hypoesthesia was present in the area of distribution of the trigeminus. By the 6th day after the onset of the ocular manifestations, the eye condition had deteriorated so pronouncedly that blepharorrhaphy was performed bilaterally. In the following days, the general and cerebral condition of the child remained grave, while there was great improvement in the right and slight improvement in the left eye. On the 10th day, despite the blepharorrhaphy, the descemetocele in the left eye perforated and was followed by emptying of the eyeball and a concurrent, unexpected aggravation of the lesions in the right eye.

During the following days, a small central descemetocele appeared in the right eye. When the infant's general condition began to improve (27 days after his admission) and the encephalitic symptoms became progressively attenuated, the lesions in the right eye tended to disappear and processes of tissue restoration

began. Twenty-five days after the onset of the ocular involvement, the condition of the right eye was greatly and definitively improved: there remained only central leukoma, which was slightly ectasic and to which a fine neovascularization arrived from the limbus. The left eye, however, was atrophic and reduced to a scleral stump. These were the ocular findings when the child, in whom sequelae of the encephalitic process were hypertonia, frequent movements of deglutition, and repeated yawnings, was discharged.

In a follow-up 3 months later his general condition was excellent, his psychic condition apparently normal, and a moderate eczema of the face was still present. The eye findings were the same. During the illness, treatment had consisted of the administration of large amounts of antibiotics, vitamins, antipyretics, placental extracts, and an appropriate diet. For the local treatment, antibiotic ointments and mydriatics had been used with little success. Inoculation into the cornea of rabbits of matter obtained by scraping the floor of an early vesicle of the eyelid gave results which were positive for herpes simplex on three successive passages, even when the infected matter was treated with an antibiotic. The rabbits died from a meningoencephalitic process similar to that which is seen in experimental herpetic meningoencephalitis. Cytological studies of early vesicles revealed the typical picture of herpes with the triad of haloed cells, polynuclear giant cells, and histoid elements in a high percentage. The cytological study was of great value in the differential diagnosis of Kaposi's varicelliform eruption of herpetic origin from that of vaccinic origin. The first consistent ocular finding in this case of Kaposi's varicelliform eruption involving the eye was dendritic keratitis in the cornea, with very little iridociliary involvement.

Dendritic keratitis, which is the most frequent and most characteristic among the keratites induced by the herpetic virus, can be considered pathognomonic for herpetic inflammation of the cornea. In this case, however, the dendritic keratitis was only the initial aspect of the ocular complication. Its worsening was due to the presence of a highly virulent strain of herpes virus and certainly also to the weak defense opposed by the corneal tissue to the infiltrating ulcerative process. The encephalitis, which very likely was also of a herpetic nature, no doubt also contributed to the aggravation of the keratitis as suggested by the fact that recovery was observed in the right eye when the cerebral symptoms improved. The extremely poor general condition of the infant owing to the severity of the general toxic infection may have also played a part. As to the origin of the ocular manifestation, it was impossible to establish whether the appearance of the virus or of its toxic products in the ocular membranes was exogenous or endogenous. Perhaps, in view of the fact that the encephalitis appeared earlier and that the keratitis was concurrent and bilateral, the virus may have arrived at the cornea by centrifugal route along the perineural lymphatic pathways or along the sheaths of the nerves or the axis-cylinder of the nervous fibers that from the brain reach the eye. It is also possible that the virus may have arrived from the skin or from other areas of the organism by the nervous or hematogenous route. In view of the fact that the eyelids were greatly involved

by the eruption, it cannot be excluded that the virus may have become implanted into the ocular membranes directly from the skin lesions. The eruption itself may have had an exogenous or an endogenous origin.

Comment: This severe case of eczema herpeticum is of ophthalmic interest because of the complicating severe dendritic keratitis leading to perforation of one eye. The herpetic etiology of this case was established beyond reasonable doubt. It is also noteworthy that corneal complications appeared on the seventeenth day of the disease, four days after the institution of parenteral cortisone therapy. This circumstance strengthens the position of those who maintain that steroid therapy should be avoided in all cases where herpes simplex is suspected or proved to be of etiological significance.

HENRY F. ALLEN

THERAPEUTICS

DIAMOX IN GLAUCOMA

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The carbonic anhydrase inhibitor acetazoleamide (Diamox), first available for clinical trials just two years ago, has come into increasingly wide use in the treatment of glaucoma.

Tonographic studies have showed that the primary effect of the drug was a diminution of the rate of aqueous flow without any immediate effect on the resistance to outflow. This effect could be demonstrated on nephrectomized rabbits and was, therefore, not directly dependent on biochemical changes resulting from the alkaline diuresis stimulated by the drug. In man, the diuresis can be suppressed by administration of ammonium chloride without diminishing the effect of the drug on aqueous flow.

Since the effect of Diamox is on the rate of secretion of the aqueous while that of miotics is on resistance to outflow, it was to be expected that the effect of these two agents might be additive and this was found to be the case by Becker. If aqueous flow was completely suppressed, intraocular pressure should drop to episcleral venous pressure (11 mm. Hg). Consequently, for the same percentual inhibition of flow the drop in intraocular pressure is greater the higher the pressure before the administration of the drug. In the most severe forms of glaucoma with extremely high resistance to outflow the pressure drop comes on slowly and the maximum pharmacological effect may not be reached before 12–18 hours with repeated administration of the drug. Even though the pressure drop in these cases may be quite large it may not suffice to normalize the intraocular pressure. The drug while pharmacologically effective in these cases may be therapeutically inadequate.

The reversible chemical reaction: $CO_2 + H_2O \rightleftarrows H_2CO_3$ which is catalysed by the enzyme carbonic anhydrase, proceeds at an appreciable rate even in the absence of the enzyme. Insofar as a given physiological system, for instance the aqueous secretory system, is dependent on this reaction, complete inhibition of the enzyme should not result in complete inhibition of the physiological function. In accordance with this expectation the rate of flow is reduced on adequate dose of the drug to an average of 0.8 cu. mm. per minute (to be compared with the normal flow rate of about 2 cu. mm. per minute), but further increase in the dosage of the drug does not reduce the flow rate still further. Moreover, if, for any reason the flow rate before administration of the drug is at a sufficiently low level, the drug will be ineffective in still further reducing the flow. Becker showed that this expectation was fulfilled in cases of low tension glaucoma.

The utility of the drug for the short term control of glaucoma has been attested by many authors. Particularly dramatic successes have been reported in relation to some forms of secondary glaucoma.

The hypotensive effect of the drug generally begins to wane about 6 hours after the oral administration and for continued control of glaucoma the drug generally needs to be given every 6 hours. The usual dose is 250 mg. Smaller doses more frequently administered are sometimes more effective. Maintained at these dosage levels and dosage frequencies, the efficacy of the drug seems to continue unimpaired. On the other hand, patients receiving the drug only every 12 or 24 hours often become refractory. The mechanism of this loss of pharmacological efficacy is not as yet clearly understood. Becker finds that administration of either ammonium chloride or sodium bicarbonate (2 g. 4 times daily) together with a more frequent administration of the Diamox can re-establish responsiveness to the drug.

Many patients on chronic administration of the drug complain of weakness, loss of appetite, numbness and tingling in hands and feet. In some cases these complaints are sufficiently severe to force discontinuance of therapy. Dermatitis and agranulocytosis are very rarely produced but have been reported. In spite of diminished rate of aqueous flow, cataracts or corneal lesions have apparently not been induced by the drug. Two cases of central scotoma which recovered slowly following discontinuance of the drug have been reported. Diamox is by no means a substitute for all more conventional forms of glaucoma therapy but is a useful addition to the therapeutic armamentarium. Some cases in which all other forms of treatment had been unsuccessful have been held under control without visual loss under Diamox therapy for as long as one year.

Comment: All ophthalmologists are aware of the ability of Diamox to lower intraocular pressure when systemically administered. Its chief value lies in short-term therapy, but it has been shown by a number of investigators (Linner & Friedenwald, Becker & Middleton, Leopold & Carmichael) that this agent can help in the long-term control of chronic glaucoma for longer than one year. Anyone who employs the chronic form of therapy should be well aware of the side effects and should keep the patient under close surveillance. A particularly bothersome complication has been the exacerbation of the symptoms of renal calculi in susceptible individuals.

Although this agent is known to inhibit carbonic anhydrase in the ciliary body, it has not been established definitely that this is the mechanism by which it produces its ocular hypotensive effect.

IRVING H. LEOPOLD

THE PRELIMINARY RESULTS OF THE TREATMENT OF UVEITIS WITH DARAPRIM

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The excellent results obtained by the experimental use of Daraprim in the treatment of toxoplasmosis in mice infected intracerebrally led to a clinical trial of this drug in patients with active uveitis seen in the Uveitis Clinic at the Institute of Ophthalmology. The patients concerned in this trial all receive a full ophthalmological and general medical examination and a routine pathological examination which includes tests for toxoplasmosis. When patients are considered suitable for inclusion in the trial, they are given one of two lots of tablets, according to a list of random numbers, and are instructed to take one tablet a day for a month, after which their condition is reassessed under the following headings: Visual acuity, aqueous or vitreous flare and cells, degree of injection, subjective response, and degree of total objective change. One group of tablets contains Daraprim 25 mg. and the other an inert substance, but the clinician dispensing the tablets and assessing progress does not know which contains the active substance. By this means the psychological effect of the treatment should be equal in all cases.

The first 63 patients in whom the drug was tried for a full month and for whom the pathological reports were complete were divided into four groups: (1) All those who had a positive dye test titer of 1:4 or more and who received Daraprim; (2) those who had a positive dye test but who received the inert tablets; (3) and (4) treated and untreated patients with negative dye tests. The site of the inflammation, which was anterior in 30, posterior in 20, and generalized in 13, is disregarded in the present analysis, because the numbers in the various groups would be so small as to have little significance. Later, of course, it will be necessary to analyze the results of each anatomical group, comparing the toxoplasma-positive and the toxoplasma-negative cases.

Group 1 contained 21 toxoplasma-positive patients treated with Daraprim: 16, or 76 per cent, were improved. The corresponding figures for Group 2, which contained 15 toxoplasma-positive patients given inert tablets, were 8, or 53 per cent; for Group 3, containing 15 toxoplasma-negative patients treated with Daraprim, they were 7, or 47 per cent; and for Group 4, containing 12 toxoplasma-negative patients given inert tablets, they were 7, or 58 per cent. At first sight it appears that the results in the first group, the only one in which a response to treatment was likely, are definitely better than those in any other group. However, the number of cases in each group is relatively small and if the figures are tested statistically the results are not so encouraging. Using the chi^2 test, a comparison of the first group with any other single group gives results that could easily be accounted for by chance. If, however, the first group is compared

with all the other groups combined, the probability that the apparent improvement in the first group is due to chance alone lies between 5 and 10 in 100. While this degree of probability does not in itself warrant the statement that Daraprim is undoubtedly having an effect on uveitis in these patients, it certainly does not exclude the possibility. Similarly it is not possible to argue from the results that, as there has been an improvement in the toxoplasma-positive patients treated with Daraprim over those with a negative toxoplasma reaction, then some of these cases are due to toxoplasmosis; but again this possibility is not excluded by the results. Continuance of the trial therefore appears to be worth while, although the dose of drug given may have to be modified. Recent reports have suggested that Daraprim gives good results when given in higher doses. Unfortunately, however, it is not free from toxic effects, and in one case in this series it had to be discontinued on account of a decreasing white cell count.

The trial is still under way but all patients with a positive dye test are now receiving a course of Daraprim if they formerly received inert tablets.

Comment: This excellent report by Smith and Perkins is a very timely one. All ophthalmologists are interested not only in the possibility of uveitis being due to toxoplasmosis but also in the potential value of anti-toxoplasmic agents such as Daraprim in the treatment of this condition.

The number of patients in this series at present is small. The authors are continuing the study, and within a short period of time the increase in number of cases will add greatly to the statistical evaluations of the study. The results with Daraprim in uveitis, although suggestive of its possible beneficial effect, are not convincing, as the authors have been careful to stress. There are many factors which require further investigation. The ability of Daraprim to get to the involved sites in the choroid has not been determined. The dosage of Daraprim required for therapy has not been determined, as the authors have suggested that 25 mgms. per day may be an inadequate test dose. Larger doses may mean that more toxic side effects may result. The value of the combination of sulfonamides with Daraprim has to be determined. The potential toxicity of this type of therapy, the present uncertainty of its value, and the difficulty of establishing the diagnosis of toxoplasma uveitis, make it appear advisable for the present that most ophthalmologists should not try Daraprim as a therapeutic test until well controlled studies such as that now being undertaken by Smith and Perkins lead to firm conclusions. Since we are dealing with therapeutic agents which may do harm for a condition in which its therapeutic efficacy has not been proved, wide-scale use in cases of uveitis should not be encouraged at this time.

IRVING H. LEOPOLD

PREDNISONE AND PREDNISOLONE IN OCULAR DISEASE

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Prednisone and prednisolone are synthetic derivatives of cortisone and hydrocortisone. They are produced by dehydrogenation of the cortisone and hydrocortisone nuclei at positions 1 and 2. Their corticoid activity is approximately three or four times that of cortisone and hydrocortisone. Sodium retention and potassium depletion are said to be unlikely with prednisone and prednisolone; consequently, the excretion of these substances in patients receiving prednisone and prednisolone is quantitatively very different from that in patients receiving cortisone and hydrocortisone, although the excretion patterns are similar.

Prednisone and prednisolone were used in a large number of patients with various eye conditions, such as conjunctivitis, chronic allergy, vernal catarrh, choroiditis, iritis, and uveitis, in order to evaluate them clinically and to compare the results obtained with those of previous therapy with cortisone, hydrocortisone, 9-alpha-fluorohydrocortisone, and corticotropin. Both drugs were used topically and systemically; systemic treatment was often accompanied by the topical use of the same drug. Initially, systemic doses as high as 80 mg. per day were utilized, with rapid decreases as the condition responded. Later, 40 mg. daily became the standard initial dosage in severe conditions and 30 mg. in those that were less severe. Fortunately, a large group of patients with chronic uveitis was available. These patients had been under treatment and observation for from one to five or more years and their response to other forms of steroid therapy was known. Using some of these as the basis for comparison, it seems that, in ocular inflammation, prednisone and prednisolone are approximately two and a half or three times as effective as cortisone or hydrocortisone in the same dose.

Preliminary evaluation of the patients for whom sufficient informative data are available indicates that prednisone and prednisolone are clinically superior to cortisone and hydrocortisone when employed topically in the eye. Systemically, their effect in ocular conditions is much the same as that of cortisone and hydrocortisone, but smaller doses are required. The incidence of important side effects in this series of patients was not significantly less than with other steroids.

The results of prednisone and prednisolone therapy depend on an understanding of the basic rules governing the application of steroid therapy in ophthalmology. The indications for the use of this therapy are symptomatic—edema and inflammation, regardless of cause. The known contraindication is dendritic ulcer (herpes simplex) of the cornea. This must not be confused with herpes zoster, which is an indication. Topical therapy is indicated in all external conditions (those which can be seen with the naked eye) and in most cases of ante-

rior uveitis (iridocyclitis). In this last condition, it is advisable to shorten the duration and intensity of the disease by the use of systemic hormonal-steroid therapy for the first several days of the acute process, on an ambulatory basis. Topical therapy is valueless when the disease process is located behind the ciliary body (posterior uveitis [choroiditis], optic neuritis). In such cases, systemic use of the various compounds is essential if success is to be achieved.

There is no such thing as a "course" of steroid therapy; the daily dose and duration of treatment are individual in each case and depend on the response of the patient. Initially, one must use an amount large enough to suppress the disease process, and then keep it suppressed with gradually decreasing doses until the patient becomes completely free from signs and symptoms when off medication. Increased symptoms indicate an increase in dosage, and a decrease in symptoms may be met with decreased doses. In external disease, such as an eyelid allergy, topical therapy alone may be insufficient. The addition of from 5.0 to 10 mg. daily in three or four divided doses may turn the tide. The most common errors are the use of topical therapy when systemic is needed, and initial doses that are too small.

Comment: Dr. Gordon, through his vast experience with steroid therapy in ophthalmology, has become impressed with their great value in controlling ocular inflammation and edema regardless of cause. He has stressed the necessity of fitting the dosage of steroids to the individual patient rather than using a blanket prescription for all. One should not regard steroid therapy as failing until he has used an adequate dose by the proper route of administration. Although prednisone and prednisolone do not cause the same degree of sodium retention and potassium depletion as encountered with the earlier employed steroids, they do produce undesirable side effects. Fortunately these are not great, but all ophthalmologists must be aware of these in any patient who is going to be on this therapy for a definite trial period. The same undesirable side effects that were encountered with earlier steroids are still met with the use of prednisone and prednisolone therapy. Sufficient time has not elapsed since the introduction of these compounds to be certain of the incidence of undesirable side effects that will be encountered with these agents, e.g., there are reports of peptic ulcers, psychoses, hypertension, moon-facies, increase in supraclavicular fat pads, acne, alterations in hirsutism, alterations in vasomotor stability, and gastrointestinal symptoms such as cramps, bloating, etc. At present it appears that these agents have a proportionately greater diabetogenic effect than cortisone and hydrocortisone. Although all investigators in ophthalmology have tried these agents and feel that they are effective in lower concentrations than that required previously with cortisone and hydrocortisone, nevertheless not all are convinced that these agents will have a greater anti-inflammatory action than the previously used steroids in adequate dosage.

IRVING H. LEOPOLD

ANTIHISTAMINES AND THE EYE: ACTION OF A SYNTHETIC ANTIHISTAMINE (ANTISTINE) ON ANGIOSCOTOMA AND ARTIFICIAL SCOTOMA OF GOLDMANN

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Studies were undertaken to evaluate the effect of a synthetic antihistamine (Antistine) and of histamine on the eye in relation to changes in the angioscotoma and Goldmann's artificial scotoma. The angioscotoma was mapped according to Magitot's technique, while the artificial scotoma was determined according to Goldmann's method, with the slight modifications suggested by Bietti. A constant decrease in both the angioscotoma and the artificial scotoma was observed after the subcutaneous administration of 0.2 gm. of Antistine. No change was observed, however, in either after the instillation of an Antistine collyrium in a 5 per cent solution into the conjunctival sac of both eyes at the rate of 1 or 2 drops every 10 minutes for one hour. The subcutaneous injection of 2 mg. of histamine, on the other hand, was always followed by dilatation of the angioscotoma and the artificial scotoma. Only in one of 12 persons did Goldmann's artificial scotoma remain unchanged after the histamine administration. A subcutaneous injection of 0.2 gm. of Antistine followed 30 minutes later by a subcutaneous injection of 2 mg. of histamine caused no change in the angioscotoma and the artificial scotoma in three-fourths of the persons studied. In the remaining one-fourth, both the angioscotoma and the artificial scotoma were dilated. The antihistaminic action of Antistine was thus capable of blocking that of histamine. The authors emphasize the consistency of the results obtained on the angioscotoma and the artificial scotoma and they state the decrease in both by Antistine suggests that its action is strictly vascular.

Comment: The term "antihistamine" has shortcomings in that it implies that all of the actions of histamines are blocked and that there are no significant actions other than that against histamines. Both of these statements are equally untrue. However, most of the many antihistaminics have been shown to have a widespread antagonism to many of the actions of histamines in various species of animals. For example, they antagonize the capillary dilatation and flare phenomena in man and various animals. They protect laboratory animals from anaphylactic shock and they will protect animals against lethal doses of histamines, but almost all of the antihistaminics have other actions such as an anesthetic effect. Many of the antihistaminics potentiate the action of epinephrine. Some have a definite adrenolytic action.

Antazoline, or Antistine, has been reported to inhibit the activity of hyaluronidase. The present authors have demonstrated that antazoline, when administered systemically, may produce some vasoconstriction of the retinal vessels as determined by angioscotometry and that histamines, similarly administered, cause a dilatation of vessel or widening of the angioscotoma. The data does not allow one to exclude a possible effect on tissues adjacent

to the vessels as being responsible for the alteration, although this seems unlikely. The data also indicates that locally instilled preparations fail to reach the retinal vessels. It is conceivable that, if some of the vascular diseases of the fundus are related to an anaphylactic reaction causing release of histamines, systemically administered antihistaminics might be of beneficial effect. Although antihistaminics have been with us for many years, there has been very little evidence of their favorable effect on fundus diseases. It would be interesting to see these studies repeated where direct observations of the retinal vessels could be made.

IRVING H. LEOPOLD

ECONOMICS, SOCIAL AND LEGISLATIVE

A SYSTEM OF VISION TESTING FOR MOTOR VEHICLE DRIVERS

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How well one must see in order to drive safely is a difficult matter to decide. The total function of sight involves not only perception, but also interpretation. The difficulty in assessing the relationship of sight to driving competency is that interpretative action of the intellect may compensate for defects in perception. The opposite, of course, is also true, for even the most refined visual perception will not be adequate for driving safety if interpretation is disturbed or defective. Thus we have an experimental situation involving three variables: perception, interpretation, and the driving situation. To study the relation between visual perception on the one hand and driving ability on the other, the factor of interpretation must be controlled. Unfortunately, controlled studies, which are essential to the establishment of rational visual standards for drivers, have not been carried out, because it is extremely difficult if not impossible to control this factor of interpretation. But this is not the only difficulty: visual functions cannot be measured exactly. Various studies of visual acuity and heterophoria measurements have shown that while visual acuity tests are relatively high in reliability, heterophoria measurements are less repeatable.

Though a highly scientific approach is impossible, yet by keeping the basic principles in mind and using what is known at present, it should be feasible to arrive at some reasonable opinion concerning the manner of testing the vision of motor vehicle drivers. With the passage of time and the accumulation of correlated data from thousands of cases, it should be possible in time to reduce the variables so as to arrive at an increasingly accurate standard of vision for the average person driving under average conditions. The test procedures must have a high test-retest reliability and be easy for relatively inexperienced persons to administer to large numbers of people. Most authorities consider visual acuity, fields of vision, ocular muscle balance, color vision, and night vision to be the factors most important to the motor vehicle driver.

A certain level of visual acuity should be required of all drivers. The European standards adopted at the Thirteenth International Congress of Ophthalmology held in Amsterdam in 1929 require visual acuity of 20/20 in one eye and 20/30 in the other for public service and taxi drivers (with varying provisions for corrective glasses); for drivers of private cars binocular visual acuity after correction must be 20/60, with 20/200 permitted in the worse eye. Seven of the 10 provinces

in Canada require visual acuity tests, the permissible level ranging from 20/40 to 20/70. In 46 of the 48 states of the United States, visual acuity standards of from 20/30 to 20/70 are required. From the medical point of view, a visual acuity test is the starting point in the examination for all ocular diseases and so for this reason alone it should be included.

The opinion held by Berens, that a field of vision of less than 104° tends to make for unsafe driving, is in substantial agreement with the recommendations of the Thirteenth International Congress of Ophthalmology. For this reason and because the visual field is often affected in ocular disease, it seems that a peripheral field test, in the horizontal meridians at least, should be made. Faulty response to this test, which is relatively accurate and reliable, should be considered cause for referring the candidate to a competent ophthalmologist.

Measurement of ocular muscle balance should be left out of the visual examination for the present for two reasons: first, there is no consistent evidence to show that either heterophoria or heterotropia has any relationship to the ability to drive safely and, second, there are no simply applied tests of high reliability for these factors. Persons complaining of diplopia should be referred for eye examination by a competent ophthalmologist.

The visual tests for stereopsis are even more unreliable than those for heterophoria. Moreover, it appears likely that stereopsis has little if any relation to the ability to drive safely. All such tests, therefore, should be left out. Accurate tests for night vision are not easy to apply, but the same purpose can be accomplished by referring all patients with defective visual acuity and fields, or either one, to an ophthalmologist. In this manner, pathologic conditions leading to night blindness will be discovered. As for elderly drivers, it is a question whether they should be permitted to drive at all.

From this discussion, it may be seen that the only defensible type of examination is one which involves no more than tests for visual acuity and visual fields in the horizontal meridian, supported when necessary by an eye examination by an ophthalmologist. The procedure outlined in the basic pattern for testing laid down by the Thirteenth International Congress of Ophthalmology, whereby different levels of vision are required according to the difficulty and responsibility of the driving situation, has much to recommend it. Certain modifications, such as the elimination of color vision tests, should of course be made in the light of the advances of the last 25 years. Table I summarizes the

TABLE I

Recommended Visual Requirements

Type of license	Corrected visual acuity	Refractive error (eq. power)	Fields (horizontal)	Re-exam.
(1) Drivers of heavy transport.	20/30 20/30	Not more than 4 D.	Full (140°) each eye	Every 3 years
(2) Drivers of light transport..	20/30 20/60	Not more than 5 D.	Full (140°) each eye	Every 3 years
(3) Private drivers.				
(a) Unconditional.....	20/40 20/100	Not applicable	Full (140°) in one eye; not less than 100° in other	Every 3 years
(b) Conditional. Monocular, strabismus and cataract candidates licensed on their merits.				

requirements to be recommended after the necessary modifications have been made.

Candidates who are blind in one eye, have a strabismus, or have had a cataract extracted deserve special attention. Each case should be considered on its merits by an experienced ophthalmologist, because only a properly trained, highly experienced ophthalmologist can make a scientifically justifiable and morally equitable decision in such cases.

Comment: The psychologist's efforts to identify "accident prone" drivers have shown this to be an elusive goal. Batteries of tests give better predictions than any single test, but even the use of a battery of tests including the most reliable tests of visual efficiency has given predictions that were valid only on a group basis and not to a practical degree for individual drivers (Forbes, T. W., In Fryer, D. H. and Henry, E. R. (eds.) Handbook of Applied Psychology, Rinehart, New York, 1950). The joint use of tests together with accident records would probably increase the accuracy of prediction and make it possible to eliminate some of the more hazardous repeaters from streets and highways on the basis of objective evidence.

In this article Nicholls takes a refreshingly realistic position on the subject of visual tests for drivers. Since complex visual performances are involved in driving and only a few necessary components of these processes can be measured reliably, the practical decision of where cut-off points should be placed on tests of acuity, visual fields and other sensory-perceptual components is being made well in advance of information regarding the exact contribution of each component to the driver's ability. Society can and should demand the best expert opinion as to how visual screening tests can protect its members against that group of unsafe drivers whose defective visual capacities are at the root of their ineptness. Research should then be directed (1) toward the more precise determination of the appropriate cut-off points on existing visual tests, and (2) toward improving tests of more complex perceptual and judgmental processes that contribute to skillful driving. The experience gained and the methods developed in traffic research laboratories at Harvard University, Northwestern University and Iowa State College (to mention a few pioneering institutions) should be utilized in an interdisciplinary program aimed toward these objectives. Engineers and law enforcement officers, as well as ophthalmologists and psychologists, could profitably cooperate to increase the rate of progress being made in improving this man-machine-highway interaction process.

AUSTIN H. RIESEN

Basic Sciences

ANATOMY

ANASTOMOSES BETWEEN THE RETINAL AND CILIARY ARTERY CIRCULATIONS

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The hypothesis that there may be anastomoses between the retinal and ciliary artery circulations near the optic nerve was investigated by examination of casts of the ocular circulation prepared by the intravascular injection of Neoprene latex according to Ashton's method.

There is no evidence that uveo-retinal vascular anastomoses occur within the normal globe, and, indeed, it is known that Bruch's membrane, in its healthy intact state, forms an impenetrable barrier to the passage of blood vessels, so that, except in certain pathological conditions when the continuity of Bruch's membrane is disturbed, there are no such anastomoses. This was verified during a recent investigation of the choroidal circulation, by an examination of Neoprene casts of the ocular vessels, and no chorio-retinal anastomoses were found even in the region of the ora serrata which has been suggested as a possible site of anastomosis from time to time. Attention has been concentrated, therefore, on the region of the optic nerve, particularly near the optic nervehead where the ciliary and retinal vessels pass close to one another as they enter the globe.

It is important to distinguish clearly these uveo-retinal arterial anastomoses from the so-called cilio-retinal arteries which have been described by many observers. Uveo-retinal arterial anastomoses constitute a direct link between the ciliary arterial circulation and the main stem of the retinal artery, whereas cilio-retinal arteries are small retinal arteries which occur in a certain number of normal eyes and are derived, not from the retinal circulation, but from the ciliary circulation through the circle of Zinn. It follows, therefore, that in the event of a sudden blockage of the central retinal artery the blood continues to flow in a cilio-retinal artery although it ceases to circulate in the main retinal arteries. However, a cilio-retinal artery is a true end-artery which supplies only a localized segment of the retina, commonly on the temporal aspect of the optic disc, and its presence is of no avail in the restoration of the circulation within the main retinal arteries. This is in contrast to a uveo-retinal arterial anastomosis which, if present on the distal side of the arterial occlusion, provides an alterna-

tive pathway for the passage of blood into the whole retinal circulation, despite the continuance of the occluding process in the central artery of the retina.

In addition to the importance of uveo-retinal arterial anastomoses from a pathological point of view, evidence has been put forward recently by Sautter and Seitz (v. Graefe's Arch. f. Ophth. 1952, *152:* 413) that such anastomoses may also have a physiological significance. In an experimental investigation on the rabbit, Sautter and Seitz found, under normal conditions, that a vital dye injected intravenously passed along the retinal artery to the lamina cribrosa where it was diverted to the circle of Zinn. This was regarded as evidence for the existence of an anastomosis between the central retinal artery and the circle of Zinn, at the level of the lamina cribrosa, under vegetative control through the mediation of a glomus apparatus at the point of origin of the anastomotic channel from the central retinal artery.

Neoprene casts of the ocular circulation of seventeen normal human eyes were prepared by the injection of Neoprene latex into the ophthalmic artery and the digestion of the ocular tissues in pepsin and trypsin. Each cast was dissected to reveal the minute details of the vessels in and around the optic nerve.

Several branches arise from the central retinal artery within the optic nerve and they may form two types of uveo-retinal arterial anastomoses. First, there are anastomoses between the central retinal artery and the arterial plexus of the pia mater surrounding the anterior part of the optic nerve, and, secondly, anastomoses between the central retinal artery and the intrascleral circle of Zinn. These anastomoses are important in a consideration of the pathological events which may follow occlusion of the central retinal artery, and in the consideration of the treatment of such cases. It is suggested that the prompt administration of oxygen may enable some of the retinal ganglion cells to survive the period when the retinal circulation is at an inadequate level, before the re-establishment of the circulation by a collateral channel.

CASE REPORT

A man aged 70 years developed an occlusion of the central retinal artery of the right eye in 1952 with practically total loss of vision in that eye.

Until March 11, 1955, the vision of the left eye had been good, but suddenly at 8 a.m. on that day his sight became cloudy and within a few minutes he could only distinguish vague outlines of objects. He was examined in the Middlesex Hospital at 11 a.m. when his vision was limited to hand movements. The retinal arteries of the left eye were markedly attenuated and there was some edema of the central part of the fundus. An occlusion of the central retinal artery was diagnosed.

Shortly after mid-day the patient was placed in an oxygen tent where an atmosphere of 70 per cent oxygen concentration was obtained with a flow of 7 litres of oxygen per minute. This was maintained for the following 72 hours. He was also given 50 mg. nicotinic acid four times daily.

On removal from the oxygen tent he was able to count fingers easily, and a few days later, when it was possible to record his vision more accurately, he

could read 6/60 corrected to 6/24 (−1). Since then his distant vision has fluctuated between 6/24 and 6/18. The visual field has remained fairly constant with a peripheral limit of about 30° as recorded on the perimeter with a 3-mm. white test object, and there are also vague areas of relative loss in the paracentral area.

There is no doubt that the ganglion cells of the retina of the left eye have suffered a considerable degree of permanent damage with complete involvement of parts of the peripheral retina and scattered involvement of the central retina. It is the implication of the central retina which accounts for the variability of the vision, and for the great difficulty which is experienced on attempting to read small print. On the other hand, when account is taken of the poor vision which usually follows occlusion of the central retinal artery and of the practically total loss of sight in the right eye after a similar central retinal arterial occlusion, the visual result must be regarded as satisfactory.

There is, of course, no direct evidence that the administration of oxygen affected the result in any way, and it is quite possible to regard the improvement in vision solely as a spontaneous occurrence. In view, however, of the hypothesis which has been put forward in the preceding paper it is hoped that oxygen therapy will be tried in similar early cases.

Comment: The author offers new evidence for an anastomosis between the central retinal artery and the uveal vascular system. The use of the Neoprene injection and cast method has led to the same findings which have been demonstrated by other investigators using a vital dye technique. Although such anastomoses are present, there is much clinical experience which suggests that this circulation is rarely adequate when the central retinal artery is occluded.

The case report describes a logical method of treatment with nicotinic acid and high oxygen concentration. In the opinion of this editor, however, the good results which follow this therapy is not adequate evidence to support the theory of collateral circulation from the uveal system. Occasional cases of apparent complete closure of the central retinal artery recover for reasons that are not known. It is quite possible that in some instances there is an incomplete block of the artery with significant angiospasm. Additionally there is also considerable question whether nicotinic acid has any vasodilating effect on the retinal vessels or the central retinal artery. There is evidence that the inhalation of high CO_2 concentrations have definite vasodilating effects on cerebral circulation, therefore, one should consider the use of high oxygen and CO_2 inhalation in patients with central retinal artery occlusion.

ALBERT N. LEMOINE, JR.

BIOCHEMISTRY

THE OCULAR MANIFESTATIONS OF HYPERCALCEMIA

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Deposits of calcium are often visible, especially on slit-lamp examination, in the conjunctiva or the subconjunctival tissues and in the corneas of persons with high blood calcium levels. In 1947, attention was focused on these deposits when they were discussed by Walsh and Howard, who described the conjunctival deposits, without giving them any specific name, as small, glasslike, crystal-clear particles within the ocular conjunctiva in the region of the palpebral fissure. The corneal deposits, on the other hand, were classified as a primary type of band keratitis characterized by hazy, grayish granular epithelial and subepithelial opacities running concentrically with the limbus on the nasal or the temporal side or both, densest at the periphery and fading out centrally. The opacities, which involved almost the entire cornea at times, were said to resemble the band keratitis ordinarily seen in association with intraocular inflammation. Clear areas within the opacities, which were thought by them to be characteristic of the band keratitis of hypercalcemia, were later described by Berliner as characteristic of band keratitis due to other causes.

According to Berliner, the most common form of band keratitis is characterized by the insidious evolution of a grayish bandlike opacity situated in the exposed interpalpebral zone. The lesions develop first as a turbid area in Bowman's zone at either the temporal or the nasal margin of the cornea or both and then spread along a horizontal line to meet centrally and form a band of opacity in which there are scattered dark round holes of various sizes. The lateral margins of the opacity are separated from the limbus by a clear zone. The older portions of the lesions become white and chalky, probably as a result of hyalinization and calcareous changes. Later, small erosions may develop in the epithelium of the cornea. A second and less common type of band keratitis occurs at the limbus and either encircles the cornea or forms an isolated superficial semilunar opaque area in Bowman's zone.

Berliner states that band keratitis may develop spontaneously in otherwise unaffected eyes or may be secondary to long-standing intraocular inflammation or exposure of the eye to external irritants. Neither he nor Doggart, who also dealt with this subject, mentioned hypercalcemia as a possible cause of band keratitis, though it may have been responsible for at least some of the cases previously so diagnosed. The term band keratopathy, suggested by Cogan and his associates, is probably a better name for the lesions in the cornea resulting from

the deposition of calcium in previously normal tissue as a manifestation of metastatic calcification.

Walsh and Howard and Cogan, Albright and Bartter were the first to recognize the similarity of the corneal and conjunctival lesions seen in a number of varied disease states and to determine that hypercalcemia was the one factor common to these disease states and, therefore, probably responsible for the ocular lesions. Opinions differ as to which lesions are the more specific, but a diagnosis of hypercalcemia may be considered in the presence of calcification in either the cornea or the conjunctiva. Apparently, the deposition of calcium in the cornea and the conjunctiva can occur rapidly in the presence of a rising concentration of calcium in the blood, and the deposits will regress gradually when the blood calcium returns to normal and remains at normal levels. In one patient with post-thyroidectomy hypoparathyroid tetany, conjunctival lesions were seen to appear after calciferol had been administered for 15 days. During this time, the concentration of serum calcium rose from 7.7 to 15.8 mg. per 100 ml. The deposits were not present in the conjunctiva on examination 5 months later. The symptoms of hypercalcemia *per se* are rather vague and nondescript. Recognition of the distinctive lesions in the cornea and the conjunctiva may serve as an important clue to the diagnosis of hypercalcemia that would otherwise be unsuspected. Metastatic calcification, in fact, may be an early and even an isolated sign of this disorder, which is present in a variety of conditions, including hyperparathyroidism, vitamin D intoxication, sarcoidosis, and the milk-alkali syndrome.

Corneal and conjunctival calcification occurring in patients with sarcoidosis has been noted by various authors; in some, it was thought to be secondary to previous intraocular inflammation, while in others it was attributed directly to hypercalcemia. The direct connection between hypercalcemia and deposits of calcium in the cornea and the conjunctiva was probably first recognized in Vitamin D intoxication in a patient who was given AT-10 (dihydrotachysterol) for the relief of post-thyroidectomy hypoparathyroid tetany in 1938. Her blood calcium rose to 14.1 mg. per 100 ml. and remained elevated for about a year in spite of the discontinuance of the AT-10. At the height of the hypercalcemia, extensive calcification of each cornea and some deposits in the neighboring conjunctiva were present. The deposits of calcium diminished gradually so that by the time the blood calcium had returned to normal levels, only traces were left. Other cases of vitamin D intoxication associated with the characteristic ocular lesions have since been reported and in most of them renal insufficiency was also present. Hypercalcemia resulting from immobilization led to ocular calcification in a case reported by Walsh and Murray, and metastatic calcification of the ocular tissues has been reported in a few patients with primary hyperparathyroidism. Band keratopathy and conjunctival lesions have been seen in various patients with renal insufficiency and hypercalcemia, some of whom had a history of excessive intake of milk and alkalis.

Histological examination of the cornea of the right eye of a patient with the milk-alkali syndrome, which had been removed three years earlier because of

painful glaucoma, showed almost complete infiltration with calcium. Opacities were likewise present on the nasal and temporal margins of the left cornea. In the right cornea, the posterior surface and the stroma were not abnormal. Bowman's membrane was intact and appeared normal in its axial portion but became increasingly calcified toward the periphery. The calcification was densest at the limbal extremity of Bowman's membrane, and spread into the superficial stroma. Anterior to Bowman's membrane was a newly-formed connective-tissue membrane in the anterior portion of which were calcific plaques. Some of these plaques were erupting through to the surface of the cornea. Areas of calcification were present also in the superficial layers of the sclera over the ciliary body. The clear lacunae seen clinically within the areas of corneal opacity in cases of calcification may well result from the sloughing of calcific plaques that have erupted to the surface. Similar plaques have been seen in other cases of corneal calcification.

Although both hypercalcemia and hyperphosphatemia seem to be generally regarded as prerequisite to the production of metastatic calcification, there have been some exceptions to this rule. The problem of the mechanism of metastatic calcification has, therefore, not yet been entirely resolved.

Ordinarily, since the corneal opacification accompanying hypercalcemia does not interfere with vision, and since it has a tendency to regress when measures are taken to reduce the hypercalcemia, local treatment of the cornea is seldom indicated. In the few cases in which vision is hampered or the eyes are irritated by spontaneous extrusion of the deposits through the corneal epithelium, the deposits can be successfully removed by treatment with a chelating drug—the disodium salt of ethylene-diamine tetraacetic acid adjusted (to neutrality) with sodium bicarbonate.

Comment: Deposition of calcium in the body may conveniently be divided into two types: (I) the normal process perhaps better called ossification, and (II) the pathologic process known as calcification. It is noteworthy that in both cases the calcium is laid down as the phosphate and carbonate in a fixed ratio.

The second process, calcification, may again be subdivided into (A) deposition in previously damaged tissues and (B) deposition in normal tissues. Type A is a common occurrence throughout the world of biology. In ophthalmology we are most familiar with band keratitis in degenerated eyes, the increase in calcium in a dying lens, the calcification of intraocular tumors and of atheromatous carotids. In the plant world one thinks immediately of the fascinating petrified forest of our own Southwest. The mechanism of this generalized process is unknown but it is probably due to an increased alkalinity of dying tissues (due to lack of production of CO_2) which favors the precipitation of calcium salts from an already saturated solution and secondly the release of calcium from Ca-proteinate combinations due to hydrolysis of tissue proteins. This newly available calcium exceeds the solubility potential of extracellular fluid and precipitates out.

The second subgroup (B), precipitation of calcium in previously normal tissues, forms the entity known as metastatic calcification. This occurs primarily in hypercalcemia and the source of excess blood calcium is usually bone. The normal blood value for calcium is about 10 mg./100 cc. plasma. Of this about half is physiologically active. Therefore a 70 kg. man with 3 kg. of plasma would have a total of 300 mg. of calcium in his blood-

stream. This minute amount exists in an uneasy equilibrium with a vast reservoir of calcium in bone. To maintain this unbalanced equilibrium a very delicate balance exists between calcium intake, calcium excretion, and the levels of vitamin D and of parathyroid secretion in the body. A disturbance of any of these factors results in aberrant deposition of calcium in the body as illustrated by the authors in this article.

A definitive monograph on this subject is that of Albright (of Albright's syndrome) and Reifenstein, "The Parathyroid Glands and Metabolic Bone Disease," The Williams & Wilkins Co., Baltimore, 1948.

DAVID SHOCH

BACTERIOLOGY

PROPHYLAXIS IN THE EYES OF NEWBORN INFANTS A COMPARISON OF SILVER NITRATE AND ERYTHROMYCIN

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Although the immediate instillation of silver nitrate into the eyes of the newborn, initiated by Credé three-quarters of a century ago, was the first successful method for the prophylaxis of ophthalmia neonatorum and although it is now required by law in many states, it has always failed in a small but definite percentage of cases. The actual reduction of gonorrheal ophthalmia from the shocking figure of 10 per cent to 0.25 per cent, however, would probably forestall much of the criticism directed against silver nitrate were it not for the fact that it frequently causes chemical irritation of the conjunctiva and that blindness may result from the use of deteriorated or overstrong concentrations. The therapeutic value of silver nitrate is also open to question because, unlike the sulfonamides and antibiotics, it has no true therapeutic effect on the gonococcus.

Trials that have been carried out during the last eight years, using several of the sulfonamides and antibiotics both locally and systemically as prophylaxis in the eyes of newborn infants, have shown that these drugs are as good as or better than silver nitrate in effectiveness and that they produce much less local reaction. Moreover, deterioration of these compounds, while presumably reducing their effective therapeutic value, does not render them injurious to the corneal tissues. Increasing recognition of the potential dangers associated with the use of silver nitrate led the St. Louis Pediatric Society and the St. Louis Gynecological Society in 1953 to propose a study of the problem in five teaching hospitals in the city of St. Louis. Permission for the investigation was secured from the Missouri Division of Health, and the Health Department of St. Louis also sanctioned and cooperated in the program.

The choice of an alternative to silver nitrate was a difficult one. Although the proposal for irrigation of the eyes of the newborn with sterile water or saline solution only is a provocative one, it was not considered feasible for over-all use at the present time. Penicillin ointment had previously been demonstrated by various workers to be an effective, non-irritating preparation that is probably the agent of choice in the well-regulated delivery room. In granting permission for this investigation, however, the Missouri Division of Health was interested in a substitute that could be used in home as well as in hospital deliveries, and by midwives as well as by physicians. Such a preparation would have to be stable for long periods of time at ordinary indoor and outdoor temperatures. Moreover, it seemed that a drug which would be effective against

the gram-positive organisms commonly cultured from the newborn infant's eye as well as against the gonococcus would be desirable. Accordingly, erythromycin ophthalmic ointment carrying a fifteen-month dating and requiring no refrigeration was selected. The possibility of sensitization was discounted in the light of the apparent anergy of the early neonatal period.

From March 1, 1953, then, to June 1, 1954, 1 per cent silver nitrate solution in drops or ampuls (according to the existing practice of the participating hospital) was alternated with erythromycin ophthalmic ointment as the prophylactic agent in a total of 12,599 infants born in the five hospitals. No case of gonorrheal ophthalmia was observed in the entire group, and none appeared after discharge from the hospital. The infants receiving silver nitrate numbered 5,489; the other 7,110 received erythromycin ointment. Records of the number and severity of conjunctival reactions were kept in 2,333 of the infants. All observers were impressed with the superiority of the antibiotic over silver nitrate as shown by the greatly reduced number of reactions and even more by their lessened severity.

Erythromycin ophthalmic ointment was found to be easy to apply, stable for long periods without refrigeration, and effective in protecting the eyes of the newborn.

Comment: The present report and others cited by the authors point to the conclusion that silver nitrate is no longer the drug of choice for the prophylaxis of ophthalmia neonatorum. The problem of deciding which one of several effective antibiotics is the drug of choice will doubtless be the subject of controversy for many years to come. A 2 per cent incidence of redness and swelling plus discharge following the use of erythromycin ointment gives pause to wonder whether this drug is the best available for the purpose.

HENRY F. ALLEN

THE CYTOLOGIC DIAGNOSIS OF TRACHOMA

PHILLIPS THYGESON

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Rev. Internat. Trachome, 1955, *32:* 421–436

The diagnosis of trachoma at onset and before the development of gross cicatrization and pannus is often difficult. As a result, cases of nontrachomatous follicular disease are often diagnosed as early trachoma in countries with a high trachoma index, and in countries with a low trachoma index the trachomatous nature of early or atypical cases may not be recognized until late changes occur.

There is, therefore, a very real need for a reliable laboratory diagnostic method. Cytologic diagnosis based on the microscopic examination of conjunctival scrapings and follicular expressions has proved valuable in the author's personal experience in (1) the incipient or prototrachomatous stages of the disease, (2) cases in which the underlying trachoma is obscured by overwhelming secondary bacterial infection, (3) atypical cases in which either the conjunctival or the corneal changes are minimal, and (4) borderline cases occurring in a heavily trachomatized population.

With the exception of the inclusion bodies of Halberstaedter and Prowazek, the cytologic changes of trachoma have been more or less neglected; even in the few works in which the subject of cytology is considered in detail no attempt has been made to present a critical analysis of the diagnostic reliability of cytologic findings as compared with biopsy or clinical findings. The present study, therefore, was undertaken to determine the value of cytological examination, both as a diagnostic procedure in trachoma and as a means of estimating the activity of the disease.

The inclusion bodies are admittedly the most important cytologic finding in trachoma. They are in fact the first recognizable sign of trachomatous infection and can be demonstrated in the incubation period before the development of any clinical signs. Unfortunately, their diagnostic value is limited, first by the fact that morphologically identical inclusions occur in inclusion conjunctivitis (which at one time led mistakenly to an identification of the two diseases), and second by the fact that in trachoma of low activity inclusions may be so few in number as to escape detection in the usual single-slide examination. However, by means of the multiple scraping technique in which material is taken carefully from the various conjunctival areas showing greatest infiltration, inclusions can usually be found even in cases of minimal activity. When typical inclusions are found, the diagnosis is limited to trachoma or inclusion conjunctivitis, and the degenerative cell changes associated with trachoma regularly seem to provide a means of differential diagnosis between the two.

Next in importance among the cytologic findings in scrapings are Leber cells (large mononuclear phagocytes) in numbers, germinal center follicle cells (lymphoblasts) with degenerative changes, plasma cells, and multinucleated epithelial cells. In follicular expressions, on the other hand, the significant findings in order of importance are Leber cells in numbers, degenerated germinal center cells (lymphoblasts), cytoplasmic debris, and greater numbers of lymphoblasts than of other mononuclear cells. In biopsy material from trachoma and follicular conjunctivitis, the degenerative changes in the trachoma follicle distinguish it from the nontrachomatous follicle. This difference can be observed just as well in expressed follicular material. In trachoma it is easy to obtain satisfactory specimens by means of ring forceps, but in nontrachomatous follicular conjunctivitis the obtaining of specimens may be difficult in the extreme because of the hardness of the follicles. In some instances, they have to be literally torn from the conjunctiva. In the author's experience, neither inclusion bodies nor free virus bodies have been found in follicular contents. Occasionally, surface

epithelial cells may accompany the follicular contents and these may contain inclusions, but no virus bodies have been found in any of the follicle cells themselves in any of the cases studied.

In this continuation study of the cytology of trachoma, which has extended over many years, cytologic diagnosis has been found to be helpful and reliable in most instances. In a significant number of cases the cytologic findings were strongly positive when the clinical findings were doubtful. In addition, cytologic studies offer much promise in the determination of cure of trachoma. Erythromycin therapy has been observed to produce changes in cytology, especially disappearance of polymorphonuclear and mononuclear leukocytes. The author, too, has found a rapid drop in the number of exudate cells to be a constant result of treatment with both the sulfonamides and the antibiotics. The inclusions have invariably disappeared by the fifth day in all patients undergoing intensive systemic or topical therapy and were usually not demonstrable after the third day. In two cases treated inadequately with terramycin, the inclusions disappeared temporarily but recurred when the medication was discontinued. Degenerative changes in the inclusions usually preceded their disappearance. The absence of inclusions in repeated scrapings, even after provocative tests with trauma, irritants, or topical steroids, has thus provided a reliable index of healing in a small series of cases. This aspect of the problem, however, needs further exploration.

Comment: The problem of the treatment of a red and irritated eye becomes more difficult each year despite the continued development of more effective methods of therapy. The explanation of this paradox appears to be in early and effective use of sulfonamides or antibiotics in the majority of eye infections, so that only the small residue of persistent and resistant cases seek ophthalmic care. Thus the usual patient with a conjunctival or palpebral inflammation when first seen has unsuccessfully tried the tetracyclines, penicillin (if his pharmacist is poorly read), cortisone, a sulfonamide, and one or more of the more esoteric antibiotics now available.

If these patients are going to be helped, the physician must use every diagnostic tool available. Of these tests the cytologic study of scrapings of the conjunctiva appears to be one of the most valuable but nonetheless one of the least used methods of diagnosis. This is true despite the ease with which material can be collected and studied.

Storz Surgical Instruments in Saint Louis sell a platinum spatula which can be flame-sterilized and is excellent for conjunctival scraping. This scraping should be done without local anesthesia and on a day that medication has not been instilled in the eye. The material is then placed on a glass slide and dried in air. It should then be fixed with absolute methyl alcohol for five minutes or longer. A drop of stock Giemsa solution in 1 cc. of neutral distilled water is applied for one hour. The slide is then passed rapidly through two changes of 95 per cent alcohol to remove stain debris. A cover glass should then be placed on the slide and the material studied with the microscope, using the oil immersion lens.

Thygeson has done much in recent years to aid in the recognition of conjunctival disease. His paper condensed here is but another example of the information which can be obtained by his methodical system of study. One of the best papers available on the diagnosis of conjunctival disease is his article in Beren's, "The Eye and Its Diseases." (W. B. Saunders and Co.) If the principles laid down by him there were routinely followed, conjunctival disease would be treated far more scientifically and effectively.

OPTICS

THE PHYSIOLOGICAL BASIS OF SENSORY FUSION

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The assumptions on which the present hypothesis is based are (1) that a point-to-point relationship exists between the retinal functional units and their respective end-stations (ganglion cells) in the occipital cortex; (2) that pairs of ganglion cells representing the end-station of the visual pathway proper of the right and the left eye are physiologically coupled; (3) that the so-called retinal correspondence is the representation of and the consequence of this sensorial correspondence (coupling) in the visual cortex; (4) that this coupling is innate (anatomically preformed) and that potential couplings exist not only between corresponding but also between disparate cortical ganglion cells; and (5) that the physiological significance of the corresponding cortical ganglion cells is to establish and maintain a surface of reference (Kernfläche of Hering) in relation to which, in front of or behind, all other points in the subjective visual space are localized.

Objects lying on the horopter will stimulate corresponding cortical cells. Those lying outside the horopter, on the other hand, will stimulate non-corresponding or disparate cortical cells. The distinction between far and near in relation to the horopter depends, then, on the stimulation of disparate cells and the perception of stereopsis is manifest only if the identical inputs reaching the right and left cortical cells can be integrated, i.e., if the coupling of disparate cortical cells can be brought into action, or, expressed in other terms, if the objects are localized inside Panum's area, which is a measure of the maximal disparity compatible with single binocular vision.

The probability of coupling (facilitation of transmission) between disparate cells varies inversely with the disparity. If the disparity is too great, diplopia occurs, but coupling may still be possible in which case the diplopic images are perceived with stereopsis. Coupling of disparate cells receiving unidentical inputs does not occur. Such inputs do not represent physiologically adequate stimuli, and have no perceptual importance (or meaning); on the contrary, coupling would destroy the isomorphism between objective and subjective visual space. Ordinarily, the cortical ganglion cells representing the right and the left eye are coupled together in sets of two, but under special conditions one cell in one "layer" may be coupled with two or more cells in the other "layer." When the stimulus contains unpaired elements, these elements will be spatially indetermined unless they can be coupled to a set of paired elements. The condition

for such a coupling is that these inputs must be identical. In addition, the disparity between the paired and the unpaired input must be below a certain threshold. If this is the case, the input in the corresponding cells (paired input) will determine the horizon and the input in the disparate cell or cells (unpaired stimulus) will be "visualized" in front of (or behind) the horizon. Whether the unpaired element is coupled to one or the other of two sets of paired elements depends on the dimensions of the respective disparities: ordinarily, the shortest coupling will take place. This principle, however, is subject to certain restrictions, because the couplings are largely determined by the whole context of the objective space. If the binocular clues are at variance with the monocular clues, the latter will tend to dominate the percept. The integration of the identical input of corresponding, or disparate, cortical cells probably takes place as a convergence from two or more such cells to a common ganglion cell of higher order.

The dimensions of the potential couplings vary between individuals and can be altered by training, fatigue, intoxication, and other conditions. The magnitude of the couplings decreases during intoxication and the unintegrated inputs are transmitted independently and become present in perception, so giving rise to confusion (the *hintereinandersehen* of Hering). This functional independence between the two eyes and their respective cortical representation is demonstrated in pure form in persons with horror fusionis, in whom even the integration of identical stimuli arriving in corresponding cells cannot be effectuated. Both sets of stimuli become present in perception and behave in every respect as separate entities.

Besides their importance in regard to sensory fusion, the potential couplings presumably have an importance as originators of motor-fusion. The fusional amplitudes, the dissociated movements of the eyes (vergences), are examples of motor-fusion. It seems reasonable to suppose that the impulse for a fusional dissociated movement is to be found in the potential couplings of the disparate cortical ganglion cells. With increasing disparity of the identical input, a motor impulse is necessary to prevent the disparity from increasing beyond the threshold at which diplopia occurs. An impulse is therefore transmitted to the center of ocular movements which compensates for the increasing disparity, i.e., brings the input back to corresponding or only slightly disparate cells in which sensory fusion can be accomplished. The magnitude of the fusional amplitudes will consequently be a kind of measure of the effectiveness of the potential couplings, with the reservation that it is also a measure of the effectiveness of the motor reflex-arc.

The inhibitory activities artificially demonstrated in retinal rivalry must be looked upon as a prerequisite for the binocular integration of disparate stimuli but the assumption that suppression or replacement of one of the paired stimuli plays a dominant role under normal physiological conditions is not in accordance with observed facts. Observation of the simultaneous cessation of retinal rivalry and disappearance of sensory fusion and stereopsis during intoxication demonstrates that integration and suppression are virtually complementary expressions of one and the same basic process. There is therefore no contradiction

between the necessity for integration as a governing factor in the physiology of binocular vision and Hamburger's findings that lively retinal rivalry is correlated with good binocular vision and the highest grade of stereopsis. The discrimination of very small disparities demands perfect function of the synthesizing mechanism, and this implies both the integration of identical stimuli and the differentiation (inhibition) of nonidentical stimuli.

The scheme of action of the cortical mechanism of integration here presented, which may be likened to that of an electronic gear, is undoubtedly over-simplified. The fact that special compensating mechanisms of the feed-back type may be required, however, to explain various phenomena of binocular vision, such as micropsia provoked by overconvergence, does not invalidate the general principles of cortical integration on which it is based.

Comment: Even a lengthy abstract will do no justice to this important paper in which the essential facts relating to fusion, stereopsis and suppression are discussed, critically sifted and supported by the evidence of interesting old and new experiments. To this reviewer it is a special pleasure to see his own ideas about the rigid isomorphism of retinal and cortical architecture shared by another author. In this view, retinal correspondence is innate, "anatomically preformed" and the consequence of "coupling" of pairs of retinocortical pathways in a common "endstation." The author's ideas about the establishment of a surface of reference (Hering's *Kernflaeche*) relative to which all other points in subjective space are localized, are fully in agreement with ideas expressed in almost identical words in a book of this reviewer (published in 1952). The author's scheme of cortical function is basically similar to the one published by this reviewer and is certainly more simple than the latter. This scheme makes one easily visualize the mechanism of "coupling" (the author's term for the physiologic basis of fusion) and its limitations, the mechanism of diplopia with and without depth-perception, of suppression, etc. It makes it easily understandable that shorter couplings (representing small disparities) are more easily facilitated than longer couplings (representing larger disparities), since in the latter case transmission must obviously pass through a much greater number of ganglionic relays. His experiments make it obvious to the author that "the spatial percept is determined by the neuroanatomy and neurophysiology of the visual center rather than by the organization of objects in physical space." The cortex, as the author emphasizes, combines the double retinal input into the simplest possible perceptual pattern and it chooses, by trial and error the optimal horopter of objective space which minimizes the average disparities of the multifarious visual details. According to an interesting observation of the author, the principal reason for the relatively long time necessary to integrate complicated stereograms, is due to this "process of fitting." He quotes Charnwood according to whom too the time lapse between the presentation of disparate patterns and the final percept is due to the making of several assessments and comparisons.

In a significant section of his paper the author discusses the disadvantages of which physiologic-optical experiments suffer compared with real situations. Under normal conditions no such ambiguity of perception is liable to occur as is the plague of the usual physiologic-optic experimentation with black lines, threads etc. Differences in contour, color, contrast etc. prevent this ambiguity. "The cortex must, so to speak, be able to decide the identity or lack of identity of the inputs arriving in the two layers of ganglion cells." With those simple lines or threads it is not always easy and sometimes impossible for it to make this decision.

The most important section of the paper in this reviewer's opinion is the author's

discussion of the relative places of rivalry and stereopsis in binocular vision. As a matter of fact, he postulates that "without retinal rivalry there is no stereopsis." Verhoeff (1935) and more recently Asher (1953) denied that true fusion exists. They have devised a number of experiments to disprove the fusion theory. Charnwood (1954) aptly criticized these experiments. "When the suppression theory still has some adherents the reason must, undoubtedly, be found in the difficulty to explain the presence and the significance of retinal rivalry according to the fusion theory. Rivalry demonstrates that during certain experimental conditions one of the stimuli arriving in corresponding elements is inhibited and it is quite easy to understand that this remarkable phenomenon has attracted great interest with the result that suppression has played a far greater role in the considerations regarding the physiology of binocular vision than this concept really deserves. However," as the author emphasizes, "the experimental set-up by which the retinal rivalry, (rivalry at the junction of contours) is demonstrated is *definitely unphysiological* and the human binocular mechanism never receives stimuli of this kind during its normal working conditions." Rivalry appears when corresponding elements receive stimuli which differ in some respect. Generally it is demonstrated with objects of the crossed diagonal type or crossed bars and lines in a stereoscope and in all these cases one sees a defect in one of the contours at the crossing points. The inhibition so manifested usually changes more or less regularly from the right to the left eye with a frequency which is relatively constant for any one observer. But even for the same observer the frequency varies with the degree of contrast and, as demonstrated by Lawaetz (1939), it is the greatest when the contrast is pronounced.

Alternation (rivalry) can also be produced with color-filters rather than different contours, though with these the vast majority of observers achieve at least some degree of color mixture. It is interesting to note in this connection that people who give better than average score on a stereo-range finder have lively rivalry with high frequency of alternation and are poor on binocular color mixture. Intoxication (especially with ethyl-alcohol) decreases the intensity of retinal rivalry. In fact, it will entirely disappear with higher degrees of intoxication. In experiments on himself, the author also found that his fusional amplitudes diminished during intoxication and so did his ability to fuse disparate stereograms. He also developed considerable esophoria. As these investigations show, stereopsis and retinal rivalry are closely linked; they are, according to the author, complementary expressions of one and the same cortical mechanism.

In connection with these experiments it is quite fitting that the author discusses *horror fusionis* and publishes the history of a case in which there was no fusion, no stereopsis and complete lack of retinal rivalry with consequent constant diplopia—a case in which nature caused the same type visual response as the normal will experience in the event of severe alcoholic intoxication.

All in all, as the author emphasizes, the disagreement is rather one of terminology. Retinal rivalry experiments convincingly demonstrate the presence of inhibition the intensity of which, as the just quoted experiment shows, may be varied by different means. The inhibition is completely absent in *horror fusionis* or in the case of intoxication, present in a considerable measure in those with manifest retinal rivalry. The more the two uniocular stimuli differ, the more pronounced the tendency to inhibition. "On the other hand . . . the synthesis of a disparity-pattern into a three-dimensional percept seems absolutely impossible to understand without the acceptance of a proper integrative mechanism." In fact, the simple experiment with stereoscopic targets which the author describes makes it for him impossible "to understand or conceive how this experiment might be explained by any type of suppression theory." With this clear-cut statement the

reviewer heartily agrees. "Integration of disparate but identical inputs and inhibition of non-disparate unidentical inputs are in fact only complementary expressions of one and the same basic mechanism. . . . The discrimination of very small disparities demands perfect function of the synthesizing mechanism, and this implies both the integration of identical stimuli and differentiation (inhibition) of non-identical stimuli . . . coupling of disparate cells receiving unidentical inputs does not occur. Such inputs do not represent physiologically adequate stimuli and have no perceptual importance (or meaning); on the contrary, coupling would destroy the isomorphism between objective and subjective visual space."

Although this reviewer agrees most heartily with almost all statements found in this paper and is especially glad to see such pertinent criticism of the so-called suppression theory of binocular vision, he still must voice at least one word of doubt in connection with the author's attempts at explaining a certain group of visual phenomena and the conclusions drawn from them. These phenomena are of the type known in the literature under the name, Panum's limiting case (*"Panums Grenzfall"*)—a rather artificial experimental set-up in which there is one contour (mostly a line) presented to one eye and two similar contours presented to the other eye. As mentioned above, the author has himself rightly emphasized the ambiguity of much of physiologic optic experimentation and Panum's limiting case represents a situation which in real life can never (at least "hardly ever") occur. Much too often are the targets of physiologic optical experiments taken out of context while in real life situations "the couplings are to a great extent determined by the whole context of the objective space."

The author has in his copy of this paper underlined a sentence several times as he thinks it to be of utmost importance: "If the binocular clues are at variance with the monocular clues these latter will tend to dominate the percept." That the importance of binocular vision and stereopsis has been inflated to an unnecessary degree cannot be proven better than by nature's own way of dealing with "binocular" clues if they are at variance with those much more fundamental spatial clues lumped together under the somewhat deprecatory term "monocular" clues. (Experimental evidence to this point has been quoted in this reviewer's book mentioned earlier.)

Some interesting remarks are found in a short section of this paper dealing with the so-called Fechner's paradox. (The term is not used by the author, as the pertinent literature—some of it quoted in the reviewer's book has seemingly remained unknown to him.) He mentions the paradoxical judgement of subjective brightness when at first two identically illuminated surfaces are presented to the two eyes and then the illumination of one surface is diminished and finally extinguished. According to the very plausible explanation offered by the author, the frequency of the action potentials from the right and left eye may be different in case the illuminations are different and a possible "interference" factor between these potentials might exist manifesting itself in reduction of subjective brightness. This interference will disappear when the frequency of one set of potentials becomes zero, i.e. when only one screen is illuminated.

The reviewer can again only agree with the author's explanation of motor fusion. "It seems reasonable to assume that the impulse for a fusional dissociated movement is to be found in the *potential* couplings of the disparate cortical ganglion cells." (In fact, in his book the reviewer has spent considerable effort to explain most of all refixation movements as the direct reflex outcome of the very sensory input reaching disparate parafoveal loci of the cortical retina.) "The magnitude of the fusional amplitudes will, consequently, be a kind of measure of the effectivity of the potential couplings."

It is gratifying to this reviewer to find the micropsia of overconvergence, even if shortly,

mentioned. It necessitates, according to the author, "the assumption of a compensating mechanism of the feed-back type." This, obviously, is just another word for the "proprioception" postulated by this reviewer from his own experiments.

Finally, the reviewer is pleased to see that the author published this excellent and significant paper "*In memoriam John Benson, Lord Charnwood*," a distinguished scientist, a friend of our country and of this reviewer whom physiologic optics has, alas, so prematurely lost.

ARTHUR LINKSZ

THE METACONTRAST

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Deutsch. Ophthal. Gesellsch., 1955, *59:* 291–296

The metacontrast which was discovered by R. Stigler in 1910 consists of the following phenomenon: Two half-circles are projected immediately or in short succession without an interval during a sufficiently short, so-called submaximal period. When this is done, half-circle I seems to light up only at its periphery while the part of half-circle I which is adjacent to half-circle II remains dark. The essence of the metacontrast thus consists of the fact that the image of half-circle I is suppressed by the secondary stimulation of the adjacent field except in a peripheral crescent-shaped area.

"Maximal time" is the shortest period during which the light stimulus must exert its effect on the retina in order to have the light sensation reach its maximum of brightness. The metacontrast shows that the sensation, which is produced by a very short, i.e., by a submaximal light stimulus, reaches its maximum only a long time after the disappearance of the objective light stimulus. By a sufficiently long interval between the projection of half-circle I and half-circle II it becomes possible to see half-circle I as a homogenously bright plane, similar to the one seen when half-circle I is projected alone. The time which a sensation produced by a submaximal light stimulus requires to reach its maximum may exceed considerably the exposure period, i.e., the duration of the retinal image. According to Stigler one should therefore distinguish (1) the homophotic image which corresponds with that part of the total light sensation which is already produced during the duration of the illumination of the retina, and (2) the metaphotic image which is produced only after the disappearance of the retinal image. With very short light stimuli there will be only a metaphotic light sensation. The metacontrast may therefore be defined as the extinction of the metaphotic image of the half-circle I (which outlasts the retinal image) by the stimulus of the adjacent half-circle II.

The metacontrast was used by the author for determinations of the optical perception time. Homophotic perception time was distinguished from metaphotic perception time and from the duration of the total perception image. Optical perception time is the time between the beginning of the retinal image and its perception. Homophotic perception time is the time between the beginning of the retinal image and its perception by exclusion of the metaphotic image. In order to determine the homophotic perception time, field I must be illuminated for so long a time until it is lit up for one moment in all its parts homogenously by the immediately following field II and then disappears with the metacontrast. This is the time which is required for the stimuli which flow off from all the areas of the retina to reach the perception zone. A median value of 0.11 seconds was determined for the homophotic perception time.

In order to determine the metaphotic perception time, one must establish how long a time may pass from the beginning of the exposure of half-circle I until it will light up homogenously for one moment, if the exposure time is shorter than the homophotic perception time. For this purpose half-circle II must be projected at intervals of various length after the disappearance of field I, in order to produce the metaphotic image.

With an exposure of field I for 0.05 seconds, this field lit up homogenously for one moment only after a pause of 0.12 seconds, and then it disappeared with the metacontrast. It is concluded that in this case the metaphotic perception time is 0.17 seconds, i.e. about 0.06 seconds longer than the homophotic perception time. This shows that apparently during the existence of the retinal image the stimulus, and therefore the brightness of the homophotic image, increase more than the metaphotic image.

The duration of the total perception image can be determined from the difference between the beginning of the retinal image until the metaphotic image disappears, and the time which passes from the beginning of the retinal image until it is perceived.

The metacontrast phenomenon thus offers possibilities for obtaining a closer insight in the complicated course of the optic stimulus from the retina to the psychophysical sphere of vision. With the aid of the metacontrast it is not only possible to analyse the optic process, but it also is possible to carry out numerical determinations concerning the duration of the optic process and its individual portions, within the limits which are set to biological processes.

Comment: Metacontrast is up to now a seldom studied phenomenon discovered in 1910 by R. Stigler: One illuminates the left half of a circular test field (called I) for a short time and immediately following illuminates the adjacent half (called II) by another flash. The observer has the peculiar impression that only II and the periphery of I has been lit up while the rest of I remains dark. Had the illumination of I not been followed by illumination of II, the observer would have seen I illuminated in the expected manner, in other words, he would have seen a contour separating a bright half disc on the left from the dark field on the right. Obviously, the immediately following illumination of II inhibited the establishment of such a contour while the opposite contour—bright on the right, dark on the left—established itself unimpeded. The phenomenon is obviously

related to the one studied by H. Werner who in his classic work on contour (1935–40) established that, under certain experimental conditions, one contour overrides, so to speak, another contour of opposite direction which should have been formed in the same retina[1] (and perceptual) locus. The perceptual existence of a contour seems to require the establishment of a current, of a vectorial process, in the underlying anatomic structures; it is not the outcome of sheer static juxtaposition of active (illuminated) and inactive (non-illuminated) retinal (and cortical) units but a dynamic phenomenon with the gradient light-to-dark as its essence. Were this not the case, illumination of II following that of I within the period of the latter's after-effect, would simply add a second illuminated half disc to the illuminated first half and instead of darkness on the left and light on the right (a contour right-to-left) one could simply see a totally illuminated circular field and no contour. This explanation is certainly more acceptable than the author's assumption of "suppression of the image of half circle I by stimulation of the adjacent field except in a peripheral crescent-shaped area."

In any event, one will be grateful to the author for turning our attention to this phenomenon once more and one will with interest study the details of the time relations that are necessary to elicit or to inhibit it.

ARTHUR LINKSZ

PSYCHOLOGY

THE ROLE OF CONTENT IN BINOCULAR RESOLUTION

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Am. J. Psych. 1956, *71:* 87–91

In studies of binocular rivalry, the problem of predominance has been treated exclusively in its relation to the formal properties of the stimuli presented. Little, if any, attention has been given to the content of the discrepant patterns as a possible source of influence upon the binocular outcome. Helmholtz (Treatise on Physiological Optics) came closest to considering the influence of content when he proposed an attentional theory of binocular rivalry in which the interest-character if the objects viewed was accorded a role of some consequence. Beyond this, the literature is quite free of reference to content, and the omission is reflected in the use of such abstract stimuli as circles, squares, and colored patches.

The experiment at hand represents an attempt to study monocular predominance as a function of the orientation of familiar objects; namely, human faces. A stereoscopic arrangement was used which presented a face in the visual vertical orientation to one eye of the observer, and an inverted face to the other eye. The two monocular faces stimulated corresponding areas of the two retinas and therefore, converged upon the same portion of the binocular field.

The observer was seated at a stereoscope which was then adjusted so that a binocular pattern was observed. An upright and an inverted face were then presented and the observer was asked to describe what he saw. Twelve observers, free from eye disease, were tested four times each. Of the 48 responses given by the group as a whole, the upright face predominated in 41, the inverted in 3, and there was no clear predominance in the remaining 4. Every one of the observers reported more upright pictures as predominant than inverted pictures. There was no consistent difference between either with regard to eye or to face. The pattern presented to the left eye dominated 22 times, the pattern presented to the right eye dominated 22 times, and there was no difference in the remaining 4 cases.

The results obtained confirm the prediction that an upright face has a definite and reliable advantage with regard to predominance in the binocular field. Of primary interest is the fact that the result is visual in nature and not simply a judgment made upon two equally well represented figures.

The predominance of the upright figure is exhibited in two distinguishable ways. There is, first of all, a tendency for the upright face to predominate when the two figures are simultaneously perceived. In this case the tendency is for

the upright face to emerge as an organized figure whose appearance is marred somewhat by isolated and partial details and contours of the inverted face. These details are perceived as conflicting with, and extraneous to, the dominant impression. To a lesser extent, the reverse occurs with the inverted face emerging as figure and the upright as contributing extraneous detail. Secondly, there is a tendency for the upright figure to predominate where the two figures are perceived alternately in the field. In this case the upright figure tends to remain longer in awareness during the successive phases of alternation.

Comment: The author presents evidence on a long neglected factor in visual perception. Binocular rivalry and resolution are not often considered to be functions of cumulative experience with the specific stimulus pattern being viewed. Formal properties of stimuli as they contribute to rivalry have been studied at length, the subject's prior experience with the adult's "visual world" being held relatively constant. Engel has here held formal properties constant and made use of a highly differential frequency of orientation of the form in prior experience to determine the significance of such orientation.

The results conform well to what would be expected from the theory of early perceptual learning advanced by D. O. Hebb (The Organization of Behavior, New York: Wiley, 1949). That is to say, prior contiguities of certain discrete neural processes build up with repetition the degree to which certain contours in a particular orientation "capture" large populations of neural elements in the central visual system. As a result the more familiar visual pattern is more unified and more dominant. As Engel says: "These effects have a distinct sensory character and cannot be considered merely 'interpretive' in nature." The same perceptual learning process is demonstrated by a very different technique in a study by D. G. Forgays (*J. Exptl. Psychol.*, 1953, *45*, 165–168). Here the two sides of the visual field develop different degrees of efficiency in mediating tachistoscopic word recognition as a result of ordinary schoolroom progress in learning to read rapidly. Animal research is beginning to get at some of the very early environmental factors that contribute to the rapid discrimination of visual form. The manner in which innate response tendencies interact with repeated sequences of stimulation is a fundamental problem in comparative developmental psychology. Theoretical analyses of data now available require the assumption of the operation of principles of contiguity and frequency to account for the kinds of effects measured in the Engel experiment.

AUSTIN H. RIESEN

Classics of Ophthalmology
JAMES E. LEBENSOHN, *Editor*

ON SOME REMARKABLE, AND HITHERTO UNOBSERVED, PHENOMENA OF BINOCULAR VISION

CHARLES WHEATSTONE, F.R.S.

London

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When an object is viewed at so great a distance that the optic axes of both eyes are sensibly parallel when directed towards it, the perspective projections of it, seen by each eye separately, are similar, and the appearance to the two eyes is precisely the same as when the object is seen by one eye only. There is, in such case, no difference between the visual appearance of an object in relief and its perspective projection on a plane surface; and hence pictorial representations of distant objects, when those circumstances which would prevent or disturb the illusion are carefully excluded, may be rendered such perfect resemblances of the objects they are intended to represent as to be mistaken for them; the Diorama is an instance of this. But this similarity no longer exists when the object is placed so near the eyes that to view it the optic axes must converge; under these conditions a different perspective projection of it is seen by each eye, and these perspectives are more dissimilar as the convergence of the optic axes becomes greater. This fact may be easily verified by placing any figure of three dimensions, an outline cube for instance, at a moderate distance before the eyes, and while the head is kept perfectly steady, viewing it with each eye successively while the other is closed.

It will now be obvious why it is impossible for the artist to give a faithful representation of any near solid object, that is, to produce a painting which shall not be distinguished in the mind from the object itself. When the painting and the object are seen with both eyes, in the case of the painting two *similar* pictures are projected on the retinae, in the case of the solid object the pictures are *dissimilar*; there is therefore an essential difference between the impressions on the organs of sensation in the two cases, and consequently between the perceptions formed in the mind; the painting therefore cannot be confounded with the solid object.

It being thus established that the mind perceives an object of three dimensions by means of the two dissimilar pictures projected by it on the two retinae, the following question occurs: What would be the visual effect of simultaneously presenting to each eye, instead of the object itself, its projection on a plane surface as it appears to that eye? To pursue this inquiry it is necessary that means should be contrived to make the two pictures, which must necessarily

THE LATE SIR CHARLES WHEATSTONE, F.R.S.

occupy different places, fall on similar parts of both retinae. Under the ordinary circumstances of vision the object is seen at the concourse of the optic axes, and its images consequently are projected on similar parts of the two retinae; but it is also evident that two exactly similar objects may be made to fall on similar parts of the two retinae, if they are placed one in the direction of each optic axis, at equal distances before or beyond their intersection.

Instead of placing two exactly similar objects to be viewed by the eyes, the two perspective projections of the same solid object be so disposed, the mind

will still perceive the object to be single, but instead of a representation on a plane surface, as each drawing appears to be when separately viewed by that eye which is directed towards it, the observer will perceive a figure of three dimensions, the exact counterpart of the object from which the drawings were made.

In the instrument I am about to describe, the two pictures (or rather their reflected images) are placed in it at the true concourse of the optic axes, the focal adaptation of the eye preserves its usual adjustment, the appearance of lateral images is entirely avoided, and a large field of view for each eye is obtained. The frequent reference I shall have occasion to make to this instrument, will render it convenient to give it a specific name, I therefore propose that it be called a Stereoscope, to indicate its property of representing solid figures.

For the purposes of illustration I have employed only outline figures, for had either shading or colouring been introduced it might be supposed that the effect was wholly or in part due to these circumstances, whereas by leaving them out of consideration no room is left to doubt that the entire effect of relief is owing to the simultaneous perception of the two monocular projections, one on each retina. But if it be required to obtain the most faithful resemblances of real objects, shadowing and colouring may properly be employed to heighten the effects. Careful attention would enable an artist to draw and paint the two component pictures, so as to present to the mind of the observer, in the resultant perception, perfect identity with the object represented. Flowers, crystals, busts, vases, instruments of various kinds, &c., might thus be represented so as not to be distinguished by sight from the real objects themselves.

The same solid object is represented to the mind by different pairs of monocular pictures, according as they are placed at a different distance before the eyes, and the perception of these differences (though we seem to be unconscious of them) may assist in suggesting to the mind the distance of the object. The more inclined to each other the referent planes are, with the greater accuracy are the various points of the projections referred to their proper places; and it appears to be a useful provision that the real forms of those objects which are nearest to us are thus more determinately apprehended than those which are more distant.

A very singular effect is produced when the drawing originally intended to be seen by the right eye is placed at the left hand side of the stereoscope, and that designed to be seen by the left eye is placed on its right hand side. A figure of three dimensions, as bold in relief as before, is perceived, but it has a different form from that which is seen when the drawings are in their proper places. There is a certain relation between the proper figure and this, which I shall call its *converse* figure. Those points which are nearest the observer in the proper figure are the most remote from him in the converse figure, and *vice versa*, so that the figure is, as it were, inverted; but it is not an exact inversion, for the near parts of the converse figure appear smaller, and the remote parts larger than the same parts before the inversion.

The same image is depicted on the retina by an object of three dimensions as by its projection on a plane surface, provided the point of sight remain in

both cases the same. There should be, therefore, no difference in the binocular appearance of two drawings, one presented to each eye, and of two real objects so presented to the two eyes that their projections on the retina shall be the same as those arising from the drawings.

The preceding experiments render it evident that there is an essential difference in the appearance of objects when seen with two eyes, and when only one eye is employed, and that the most vivid belief of the solidity of an object of three dimensions arises from two different perspective projections of it being simultaneously presented to the mind. How happens it then, it may be asked, that persons who see with only one eye form correct notions of solid objects, and never mistake them for pictures? and how happens it also, that a person having the perfect use of both eyes, perceives no difference in objects around him when he shuts one of them? To explain these apparent difficulties, it must be kept in mind, that although the simultaneous vision of two dissimilar pictures suggests the relief of objects in the most vivid manner, yet there are other signs which suggest the same ideas to the mind, which, though more ambiguous than the former, become less liable to lead the judgment astray in proportion to the extent of our previous experience. The vividness of relief arising from the projection of two dissimilar pictures, one on each retina, becomes less and less as the object is seen at a greater distance before the eyes, and entirely ceases when it is so distant that the optic axes are parallel while regarding it. We see with both eyes all objects beyond this distance precisely as we see near objects with a single eye; for the pictures on the two retinae are then exactly similar, and the mind appreciates no difference whether two identical pictures fall on corresponding parts of the two retinae, or whether one eye is impressed with only one of these pictures. A person deprived of the sight of one eye sees therefore all external objects, near and remote, as a person with both eyes sees remote objects only, but that vivid effect arising from the binocular vision of near objects is not perceived by the former; to supply this deficiency he has recourse unconsciously to other means of acquiring more accurate information. The motion of the head is the principal means he employs. That the required knowledge may be thus obtained will be evident from the following considerations. The mind associates with the idea of a solid object every different projection of it which experience has hitherto afforded; a single projection may be ambiguous, from its being also one of the projections of a picture, or of a different solid object; but when different projections of the same object are successively presented, they cannot all belong to another object, and the form to which they belong is completely characterized. While the object remains fixed, at every movement of the head it is viewed from a different point of sight, and the picture on the retina consequently continually changes.

Every one must be aware how greatly the perspective effect of a picture is enhanced by looking at it with only one eye, especially when a tube is employed to exclude the vision of adjacent objects, whose presence might disturb the illusion. Seen under such circumstances from the proper point of sight, the picture projects the same lines, shades and colours on the retina, as the more

distant scene which it represents would do were it substituted for it. The appearance which would make us certain that it is a picture is excluded from the sight, and the imagination has room to be active.

If we suppose a cameo and an intaglio of the same object, the elevations of the one corresponding exactly to the depressions of the other, it is easy to show that the projection of either on the retina is sensibly the same. When the cameo or the intaglio is seen with both eyes, it is impossible to mistake an elevation for a depression, for reasons which have been already amply explained; but when either is seen with one eye only, the most certain guide of our judgement, viz. the presentation of a different picture to each eye, is wanting; the imagination therefore supplies the deficiency, and we conceive the object to be raised or depressed according to the dictates of this faculty. No doubt in such cases our judgement is in a great degree influenced by accessory circumstances, and the intaglio or the relief may sometimes present itself according to our previous knowledge of the direction in which the shadows ought to appear; but the real cause of the phenomenon is to be found in the indetermination of the judgement arising from our more perfect means of judging being absent.

We will now inquire what effect results from presenting similar images, differing only in magnitude, to analogous parts of the two retinae. For this purpose two squares or circles, differing obviously but not extravagantly in size, may be drawn on two separate pieces of paper, and placed in the stereoscope so that the reflected image of each shall be equally distant from the eye by which it is regarded. It will then be seen that, notwithstanding this difference, they coalesce and occasion a single resultant perception.

If the pictures be too unequal in magnitude, the binocular coincidence does not take place. It appears that if the inequality of the pictures be greater than the difference which exists between the two projections of the same object when seen in the most oblique position of the eyes (i.e. both turned to the extreme right or to the extreme left), ordinarily employed, they do not coalesce.

It now remains to examine *why* two dissimilar pictures projected on the two retinae give rise to the perception of an object in relief. I shall in this place merely consider the most obvious explanations which might be offered, and show their insufficiency to explain the whole of the phenomena.

It may be supposed, that we see but one point of a field of view distinctly at the same instant, the one namely to which the optic axes are directed, while all other points are seen so indistinctly, that the mind does not recognize them to be either single or double, and that the figure is appreciated by successively directing the point of convergence of the optic axes successively to be a sufficient number of its points to enable us to judge accurately of its form.

That there is a degree of indistinctness in those parts of the field of view to which the eyes are not immediately directed, and which increases with the distance from that point, cannot be doubted, and it is also true that the objects thus obscurely seen are frequently doubled. In ordinary vision, it may be said, this indistinctness and duplicity is not attended to, because the eyes shifting continually from point to point, every part of the object is successively rendered

distinct; and the perception of the object is not the consequence of a single glance, during which only a small part of it is seen distinctly; but is formed from a comparison of all the pictures successively seen while the eyes were changing from one point of the object to another.

All this is in some degree true; but were it entirely so, no appearance of relief should present itself when the eyes remain intently fixed on one point of a binocular image in the stereoscope. But on performing the experiment carefully, it will be found, provided the pictures do not extend too far beyond the centres of distinct vision, that the image is still seen single and in relief when this condition is fulfilled. Were the theory of corresponding points true, the appearance should be that of the superposition of the two drawings, to which, however, it has not the slightest similitude.

When an object, or a part of an object, thus appears in relief while the optic axes are directed to a single binocular point, it is easy to see that each point of the figure that appears single is seen at the intersection of the two lines of visible direction in which it is seen by each eye separately, whether these lines of visible direction terminate at corresponding points of the two retinae or not.

But if we were to infer the converse of this, viz. that every point of an object in relief is seen by a single glance at the intersection of the lines of visible direction in which it is seen by each eye singly, we should be in error. On this supposition, objects before or beyond the intersection of the optic axes should never appear double, and we have abundant evidence that they do. The determination of the points which shall appear single seems to depend in no small degree on previous knowledge of the form we are regarding. No doubt, some law or rule of vision may be discovered which shall include all the circumstances under which single vision by means of non-corresponding points occurs and is limited. I have made numerous experiments for the purpose of attaining this end, and have ascertained some of the conditions on which single and double vision depend, the consideration of which however must at present be deferred.

Editorial comment: In his second paper on the Physiology of Vision (1852) Wheatstone remarks: "At the date of the publication of my experiments on binocular vision the brilliant photographic discoveries of Talbot, Niepce and Daguerre had not been announced to the world. To illustrate the phenomena of the stereoscope I could, therefore, at that time, only employ drawings made by the hands of an artist; but it is evidently impossible for the most accurate and accomplished artist to delineate by the sole aid of his eye the two subjects necessary to form the stereoscopic relief of objects as they exist in nature with their delicate differences of outline, light and shade. What the hand of the artist was unable to accomplish the chemical action of light, directed by the camera, has enabled us to effect. It was at the beginning of 1839 that the photographic art became known, and soon after, at my request Mr. Talbot obligingly prepared for me stereoscopic Talbotypes of statues, buildings and living persons." In 1849 Sir David Brewster designed the lenticular stereoscope, which Oliver Wendell Holmes later modified by giving it a handle and an adjustable picture carrier. The steroscope became popular after the Great Exhibition at London in 1851 where the French displayed a fine set of binocular daguerreotypes. During the next five years, 500,000 stereoscopes were sold. Although the accuracy of the stereoscopic sense is comparable with vernier acuity, its range is comparatively

limited. With the naked eye stereoscopic vision does not extend beyond 2000 ft. The radius of stereoscopic vision is about 7000 times the interpupillary base-line. In the telestereoscope, invented by Helmholtz in 1857, the effective base-line was extended by the use of right-angled prisms with a proportionate increase in stereoscopic vision. Prism binocular field glasses and stereoscopic range finders are constructed on this principle.

Linksz, a profound student of stereopsis, has explored with penetrating insight the implications of Wheatstone's pioneering contribution. The following condensed excerpts of his evaluation is essentially in his own words: "Neither Leonardo da Vinci nor Berkeley noticed the fact that the distribution pattern of retinal images in the two eyes is different. This great discovery was Wheatstone's. He was the first to state clearly that, due to their horizontally different position, the two eyes receive horizontally different views of objects. He concluded correctly that it is the inequality of the two retinal images of an object which furnishes the means of stereopsis and he made the logical step of proving his theory by procuring for each eye a flat projection of the object as it is seen by that eye. For this end Wheatstone designed an instrument which he called a stereoscope, now usually called a haploscope. The orthoptic instruments now in use are only glorified editions of his simple contrivance. If the two uniocular images are unequal in certain respects, they are equal in almost every other respect. It is this equality, not the inequalities, that make binocular vision possible."

REFERENCE

LINKSZ, A.: Vision. New York, Grune & Stratton, 1952.

BIOGRAPHICAL NOTE

Sir Charles Wheatstone (1802–1875) was born in Gloucester, England, the son of a music-seller. At the age of 21 he established his own business in London as a maker of musical instruments; and began investigating extensively the principles involved in the various forms of musical instruments. His interest then extended to vision, light and electricity. In 1834 he was appointed Professor of Experimental Philosophy in King's College, London and was elected fellow of the Royal Society in 1836. In 1838 he presented his mirror stereoscope. The word "stereoscope" was also his invention. He is popularly known for his introduction of the Wheatstone bridge for the measurement of electric resistance (1843). Another invention was the kaleidophone which gives a visible presentation of sound; but his greatest achievement was the perfection of the electric telegraph. Numerous distinctions were conferred on him by governments, universities and learned societies. In 1868 he received both the honor of knighthood from Queen Victoria and the Copley medal of the Royal Society for his researches in acoustics, optics, electricity and magnetism. His hobby was cryptography in which he was an acknowledged expert. Though an unrivalled conversationalist, Wheatstone suffered excessively from stage-freight on facing an audience. He was fortunate, however, in having the greatest lecturer of the age, Faraday, present his papers to the Royal Institution.

REFERENCE

JEANS, W. T.: Lives of the Electricians. London, Whittaker & Co., 1887.

Reports from Abroad

UNITED KINGDOM

A larger gathering than usual, including many visitors from Europe, America, Australia and even a representative from Poland, attended the 76th Meeting of the Ophthalmological Society of the United Kingdom which was held under the Presidency of Mr. O. Gayer Morgan in London on April 26, 27 and 28, 1956.

Prior to the Annual Dinner of the Society at the Royal College of Surgeons, a Ceremonial Presentation of his Portrait, painted by Mr. Ruskin Spear, R.A., was made to Sir Stewart Duke-Elder as a token of appreciation of his contribution to Ophthalmology in general and British Ophthalmology in particular.

The cost of the portrait had been met by subscriptions from members of the Ophthalmological Society of the United Kingdom and the Faculty of Ophthalmology and it was accompanied by two silver candlesticks selected by Lady Duke-Elder.

Mr. Gayer Morgan paid a tribute to Sir Stewart's many virtues and in a reference to the portrait drew attention to "the quick, bright, determined and yet humorous eyes" and to "the mouth just about to say something quite outrageous; how did the artist know about that characteristic feature which we all expect and enjoy so much?"

In the course of a speech in acknowledgement of the tribute paid to him, Sir Stewart referred to the fact that most things one gets in life—honours, position, for example—are cold and expressionless but this occasion was warm and comforting and gave a new meaning to things like "falling in love with a woman or seeing a vision on the road to Damascus." He continued, "From now on life for me will be less of a factual routine and more of a spiritual thing; because of this that you have done to me, I will travel on with a sense of less urgency and more of peace."

The scientific proceedings opened with a discussion on the early diagnosis of glaucoma. Sir Stewart Duke-Elder referred to the social importance of glaucoma as an incapacitating and blinding disease and stressed the importance of early diagnosis and treatment in the prognosis. He laid emphasis on the importance of glaucoma clinics and he pointed out the unfortunate complexity of adequate methods of diagnosis if they are to be effective at an early stage.

Mr. P. L. Blaxter and Mr. S. J. H. Miller spoke on the symptoms and diagnostic methods. Professor A. P. Sourdille stressed the fact that vascular and

nervous disorders must be considered as factors in the causation of the disease in addition to simple hydrodynamic disturbance.

The rest of the papers but one on the first day, were also concerned with aqueous dynamics. Dr. C. H. M. Pedler spoke on the relationship of hyaluronidase to aqueous outflow resistance.

Professor Rosengren spoke on the possibility of perilimbal scleral pressure impeding the drainage of aqueous humour and he described a method of compressing the intrascleral venous plexus by the use of a suction cup causing a rise in intraocular tension.

On the second day in the opening paper, Mr. K. C. Wybar discussed the various factors which have been incriminated in the process of so-called endocrine exophthalmos.

He was succeeded by Mr. J. H. Doggart who, in his inimitable erudite fashion, discussed infantile optic atrophy with particular attention to the disposal and interpretation of unilateral optic atrophy.

Professor Edwin B. Dunphy, of the Massachusetts Eye and Ear Hospital, presented a very interesting paper on the use of radioactive phosphorus (P. 32) in the diagnosis of ocular malignancy. He stressed the limitations of the test which, if not thoroughly understood and allowed for, might lead to erroneous interpretations. He presented his experiences in over sixty cases.

Mr. Frank W. Law then discussed migraine from the physician's or internist's point of view and from the ophthalmic aspect with emphasis on the importance of the latter.

Two papers on refraction and errors thereof followed. Professor Arnold Sorsby spoke on his findings in relating refractive states to axial length, corneal power and lens power in some 341 eyes. He felt that there was some tentative evidence to show that the components of refraction are genetically determined. Mr. P. A. Gardiner feels that diet and myopia are related, and gave figures in support of his contention.

On Friday afternoon, proceedings opened with a symposium on herpetic infections of the outer eye. Mr. A. J. B. Goldsmith outlined the symptomatology and therapeutic problems involved from the clinical aspect. Dr. M. Lederman discussed the value of radiotherapy in the treatment of the known herpetic lesions and other lesions of possible herpetic origin; he emphasised that radiotherapy in this type of case should be restricted to those resistant or recurrent cases where orthodox methods had failed. Dr. J. A. Dudgeon then spoke on the virology of the conditions.

There was an interesting talk on the diagnostic value of colour fields in neurosurgery given by Mr. George Alexandra, a neurosurgeon from Bristol, in which he emphasised the advantages of using coloured objects, particularly Flame Red (Dennison 150 Crepe Paper).

On the final day, Mr. L. G. Fison gave a stimulating talk on planned treatment of retinal detachments in which he emphasised the great importance of thorough pre-operative examination of the fundus by indirect ophthalmoscopy

and the interesting possibilities opened up by the newly developed method of light coagulation in retinal lesions.

A very pleasant and successful meeting was brought to a conclusion by Mr. John Primrose who described a simple method of demonstrating a macular lesion in cataractous patients by the use of the Maddox rod; the patient may be aware of a gap when looking at the centre of the streak.

FRANK D. MCAULEY
London, England

IRELAND

The Annual Meeting of the Irish Ophthalmological Society, under the Presidency of Dr. Frank Lavery, opened in Dublin on the evening of May 10, 1956, with the delivery in Trinity College of the Montgomery Lecture by Dr. Moacyr E. Alvaro (president of the Pan-American Congress of Ophthalmology). His subject was "Etiology and Pathogeny of Uveitis."

In an opening reference to the growth of ophthalmology in Dublin—six eye hospitals were founded there during the first half of the last century—Dr. Alvaro mentioned such famous names in Dublin ophthalmic history as Sir Philip Crampton, Arthur Jacob, whose discovery of the retina gave to it the name "membrana Jacobi," and who was apparently responsible for the rodent ulcer being called Jacob's Ulcer, and Sir William Wilde, said to be the most versatile and dynamic oculist that Dublin has produced, but who is probably better known to the general public as the father of Oscar Wilde.

Dr. Alvaro referred to the fact that in the same building exactly 40 years ago the first Montgomery Lecture was delivered on the same subject by Dr. Euphan Maxwell, who happily was present today. After 40 years, opinions such as those of Ashton and Woods were still at variance on the aetiology and even the pathology of the condition.

Dr. Alvaro favors the terms granulomatous and non-granulomatous uveitis; the first differentiates the type in which the ocular tissues are penetrated by the afflicting organism from the allergic reactive type of the latter. He considers that a large number of cataracts diagnosed as senile in patients over 70 years of age are, in fact, complicated cataracts in patients who are seen too late to have their uveitis diagnosed and in whom operation often leads to loss of the eye.

A very pleasant dinner was held in the evening at Jammet's Restaurant. On the following morning clinical cases were shown. In a discussion afterwards on the Ridley lenticulus, Mr. Harold Ridley, who is a member of the Society and a frequent visitor to their meetings, gave some interesting figures of his earlier cases; of 42 extracapsular extractions replaced by his acrylic lenticulus in the years 1951–1953, 10 eyes still have vision of 20/20 or better, 14 have vision of 20/40 or better, 6 cases have 20/60, 4 lie between 20/80 and 20/120, 4 have less than 20/200, and 4 have dislocated. Of these last 4 one resulted from trauma and 3 were spontaneous, probably from damage to the posterior capsule at operation. Four lenses inserted after intracapsular extractions dislocated into the vitreous. Mr. Ridley emphasized the fact that what often appears to be a straight-forward extracapsular extraction may result in damage to the posterior capsule.

In the afternoon, in a session devoted to discussion of corneal grafting, Dr. Tom Roche (Dublin) described visits to the clinics of Panfique Francescetti and other notable exponents of the operation on the Continent of Europe, and Mr. W. B. Rycroft from the East Grinstead Plastic Surgery Unit spoke on the biological reaction in corneal grafting. The absence of vessels and the fibrous

ring at the junction of the graft and host cornea prevent such a reaction as a rule, but Mr. Rycroft recommends that the epithelium should be stripped of all donor material because it tends to set up a reaction, as shown by Maumenee, Lister and Greaves. Bi-weekly eosinophil counts are advised in the immediate post-operative phase.

On the following morning Dr. Frank Lavery in his presidential address mentioned some names of famous people from abroad who have delivered lectures to the Society, but he would like to see more contributions from the Society's members.

Dr. Meyer-Schwickerath from Bonn in Western Germany was paying his second visit to the country, having been here previously 23 years ago to learn English and, judging by his wonderful delivery, he obviously spent his time usefully on that occasion.

He lectured on his new method of causing coagulation in ocular tissue by high intensities of light. The original method was by trapping the sun's rays with a convex lens, and from that followed the carbon arc machine. The Weiss Company are at present preparing to market an improved instrument with a xenon arc lamp which can be used like an ophthalmoscope. It is not often that a lecture on a scientific subject holds the interest of an audience in rapt attention from beginning to end, but it is no exaggeration to say that Dr. Meyer-Schwickerath's talk entranced his listeners by the delightful and accomplished manner in which it was delivered and by the fascinating description of the multiple uses to which his new invention can be applied, from the sealing of retinal holes, the thrombosing of angiomatous vessels, to the destruction of malignant cells and the formation of new pupillary apertures. His lecture was like a conducted tour around a huge eyeball in Fairyland, with Leprechauns manning the switches controlling the huge searchlight that was the coagulating beam. Dr. Meyer-Schwickerath has certainly opened up new horizons in ophthalmic therapy.

The final item of the meeting was a discussion on tonography, precipitated by a stimulating paper on the tonographic studies in a case of essential iris atrophy, delivered by Dr. H. McGrath from New York. The electronic tonometer, being an American product, hence practically unobtainable in the Sterling area and impossible to have serviced here, is not a practical proposition at the moment. It was pointed out, however, that a simpler instrument (non-electronic), which is said to be more accurate and much less costly, will shortly be on the market in Europe.

Next year's gathering (16th, 17th and 18th of May, 1957) will be unique in that it will be a joint meeting with the British Society of Neurological Surgeons the first time that this Society has combined with a group from another specialty for its meeting. Dr. Frank B. Walsh from the Wilmer Institute of The Johns Hopkins Hospital has been invited to deliver the Montgomery Lecture.

FRANK D. MCAULEY
London, England

Book Reviews

INDIAN YEARBOOK OF OPHTHALMOLOGY. An Indexed Annual Review of the Progress of Ophthalmology. Edited by *Vaman D. Sathaye*, B. SC.; L. C. P. S. (BOM); M. L. C.; Member, Poona University Court, Bombay Nursing Council, Employees State Insurance Corporation, etc. *V. D. Sathaye* 502 Narayan Peth., Poona 2, India. Cloth, pp. 194, 1954.

The major portion of this new annual review is devoted to brief abstracts from American and English ophthalmic journals. A total of 119 different articles published between July, 1953 and October, 1954 have been included. In addition, there are several original papers, a section of society proceedings, and an interesting listing of the special activities of eye hospitals in India during 1954. A directory of the eye specialists in India is presented in a supplement.

YEARBOOK OF THE EYE, EAR, NOSE AND THROAT. THE EYE edited by *Derrick Vail, B.A., M.D., D.Oph. (Oxon.), F.A.C.S., F.R.C.S. (Hon.)* Professor and Director, Department of Ophthalmology, Northwestern University Medical School; Attending Ophthalmologist, Passavant Memorial Hospital. THE EAR, NOSE AND THROAT edited by *John R. Lindsay, M.D.*, Professor of Otolaryngology, The University of Chicago, The School of Medicine. The Year Book Publishers, Chicago, Illinois. Cloth, pp. 471 (Eye pp. 7–241; Ear, Nose and Throat pp. 245–458), 121 illustrations, $6.50, Series 1955–1956.

The Year Book has become firmly established as a method of keeping abreast of the voluminous literature concerning clinical ophthalmology which appears each year. The current number maintains the editorial excellence which has distinguished earlier editions. As always, the comments of the editor add a refreshing piquancy to the reviews. In several instances this comment presents information of greater clinical value than that presented in the original article.

For those interested mainly in diseases of the eye, the inclusion of a section on Ear, Nose and Throat necessitates purchase of one-half a book of no immediate interest. Although the habit of incorporating the two sections has long been established with the Year Book, it seems likely that a more valuable publication would result if the Eye and the Ear, Nose and Throat sections were published separately. This would recognize the division of the specialties which has occurred since the series was initiated and perhaps permit expansion of each section to include a wider review of the current literature. There is great need for a review of important material dealing with the basic sciences since this appears in such widely scattered sources that even the conscientious student with excellent university library facilities cannot keep apace.

Thanks however to the editorial excellence of the comments and the value of the articles selected, even the half a loaf offered is of value and of interest to the ophthalmologist desirous of reviewing progress during the past year.

POTENCIALIZACION FARMACODINAMICA EN OFTALMOLOGIA. By *Joaquin Moner Barraquer*. In Spanish, with French and English translations and German and Italian summaries. Monograph Number Three of the Barraquer Institute. Barcelona, Spain. Paper, pp. 293, 1954.

During the past decade there has been an increased use of general anesthesia for intraocular surgery. Additionally the importance of individualized and adequate medication pre- and post-operatively, whether local or general anesthesia is used, has been emphasized in numerous publications.

In the United States, particularly in institutions having physician-anesthetists, the major emphasis has been upon the control of the airway during anesthesia. Once this is profound enough to permit intratracheal intubation there is little need for the use of supplementary drugs, such as curare, to maintain akinesia. Hence the vast majority of anesthetists find no indication in their patients requiring eye surgery for different pre-operative medications or special anesthetic techniques from those required in general surgery. Research and study of the various combinations of systemically administered drugs which may be used to induce a profound state of quietude and akinesia has thus lagged in the United States although there is a lively interest in the subject in Europe and South America.

This monograph describes the author's experience with 455 patients in whom a variety of eye operations were performed with "general anesthesia without anesthetics." This state was induced by using a combination of drugs acting (1) upon the higher centers (barbiturates, ganglioplegics, etc.); (2) upon neuromuscular transmission (curare and related drugs); (3) the peripheral nervous system (local anesthetics and antihistaminics); and (4) the temperature regulating mechanism (refrigeration hibernation).

For a patient requiring maximum medication, compound Bellergal (atropine and phenobarbital?) and luminal (200 mg.) are administered the day prior to surgery. Three hours prior to surgery Finergan (an antihistaminic) and Bellergal compound are given. An hour later Dolantine (a narcotic analgesic) Diparcol (a ganglioplegic largely parasympathoplegic) and Largactil (chlorpromazine) are administered. In arteriosclerotic and cachectic individuals requiring minimal medication only Compound Bellergal and Largactil are used. Upon arrival in the operating room the blood pressure, pulse, respiratory rate and equanimity of the patient are observed and, if necessary, additional medication (Dolantine, Diparcol, Ergotamine or Nembutal) are administered intravenously to lower the blood pressure or pulse to the pre-surgical level, to normalize the rate and amplitude of respiration, or to increase the degree of sedation. Local anesthesia is induced with 2 per cent tetracaine and 10 per cent cocaine 15 or 20 minutes prior to surgery and intravenous curare is started at the same time. Oxygen is administered by an open tube on the face. Retrobulbar procaine and hyaluronidase are reserved for glaucoma with a pressure of more than 35 mm. of mercury. General anesthesia with controlled hypotension is used for orbitotomy, dacryocystirhinostomy and ptosis procedures. The use of refrigeration hibernation in ocular surgery is not described.

The monograph presents an interesting analysis of the results using a variety

of drugs for surgical analgesia, akinesia and sedation. Their use must be most carefully supervised and close and intelligent observation of the patient is required to obtain the results of Barraquer and his group without precipitating a serious mishap. Although the importance of adequate anesthesia and the contribution of pre- and post-operative medication to surgical success is generally recognized, this is the first series in which the surgical results are correlated with the adequacy of this medication.

STRABISMUS: DIAGNOSIS AND TREATMENT. By *Beulah Cushman, M.S., M.D.* Attending ophthalmologist, Passavant Memorial Hospital; Swedish Covenant Hospital, Women's and Children's Hospital, Chicago, Illinois; Associate Professor Ophthalmology, Northwestern University Medical School, Chicago, Illinois. Lea and Febiger, Philadelphia, Cloth pp. 208, $6.50, 1956.

In his foreword to this volume on strabismus Derrick Vail points out that more books and articles are needed on this subject which is far from being exhausted. One can only concur in this opinion and might add that it is desirable that an author take a definite stand in a field within which there are so many varying schools of thought.

This Dr. Cushman certainly does do. Her volume is no more nor less than an interpretation of the teachings of Duane and White. Accordingly, all motor anomalies are subdivided into anomalies of individual muscles and "center anomalies." In considering the first group the emphasis is laid on "diagnosis," meaning by this essentially the determination of overacting and underacting muscles by means of the "screen test" (prism and cover test in various directions of gaze) and the "screen comitance test." All extraocular muscles are considered, but the interest centers naturally on the vertical muscles which present the greatest diagnostic difficulties. Among the "center anomalies," which include the disjunctive acts of convergence, divergence, etc., the diagnosis is mainly based on the differentiation between excesses and insufficiencies of convergence and divergence and on the behavior of the near point of convergence. Part II of the book deals with treatment and is subdivided into a chapter on "Monocular and Binocular Functions" and a chapter on "Surgery." A special feature of the book is an appendix of 62 case histories, carefully describing the examination and treatment of each patient, following the scheme laid out in the main body of the text.

The mature, critical ophthalmologist who wishes to acquaint himself with the teaching of Duane and White may do so by consulting Dr. Cushman's book. To the student who does not have a mastery of the subject, the book cannot be recommended. Information on many topics is taken for granted. For example, the major amblyoscope and its use are not explained, but early in the book the statement occurs: "Depth perception can be demonstrated on the major amblyoscope by obtaining the objective angle in the usual way and placing third grade targets at this objective angle." Many of the technical terms are loosely employed, some are incorrect, others obsolete. The efforts made in the last fifteen years to establish a clear, generally acceptable terminology—found to a large extent in such standard works as Duke-Elder's textbook—are disregarded. This cannot help

but confuse the neophyte. There are factual misstatements as in the discussion of paradoxic diplopia and of "sursumvergence" (referring apparently to alternating sursumduction) of which the author says that "sursumvergence is effected by a simultaneous contraction of the elevators of the eye or the depressors of the eye." In the description of torsional diplopia we read: "the superior oblique normally intorts, but if it is paretic it would extort and the image would be projected as intorted." Of secondary deviation it is stated that "this overaction is secondary to its associate muscle underaction and is explained by Sherrington's law of reciprocal innervation." One wonders what someone, unacquainted with the concept of convergence insufficiency, would make of this definition: "Convergence insufficiency, according to Duane, is that condition in which the parallel movements of the eyes are normal, but the associated movement to which simultaneous contraction of the internal rectus muscles should be added for near is reduced."

The last two statements are also examples of the many awkward and inelegant sentences which add to the difficulty of reading the book. This criticism should be addressed largely to the editors of the publisher whose task it is to assist the author in putting the text in the proper form. They must also be held responsible at least in part for the relatively large number of typographical errors and some misspellings (myectomy, for example, is spelled "myemectomy" throughout the book and the index).

The chief objection to the book *as a text* is its onesidedness and its lack of completeness. It is surprising that one cannot even find in it a discussion of the newer work of such men as H. W. Brown, Scobee and Fink. The subject of accommodative strabismus is mentioned only in a cursory manner and all sensory and neurologic aspects of the neuromuscular anomalies are passed over in virtual silence. This is intentional and derives from the purpose of the book, but it also limits its scope severely. There still would seem to be room for more books on the subject of strabismus.

HERMANN M. BURIAN

Current Review

PSYCHOSOMATIC OPHTHALMOLOGY*

T. F. Schlaegel, Jr.

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With the collaboration of

Millard Hoyt

Instructor in Psychiatry, Indiana University School of Medicine

Most important, in treatment of psychosomatic disorders, is the doctor-patient relationship; the development of a warm interest in the patient. One need not be a pharmacologist to treat a patient with atropine; he need not be a microbiologist to prescribe chloromycetin; and he need not be a psychiatrist to provide psychotherapy.

THE DOCTOR-PATIENT RELATIONSHIP

Although it is the basic ingredient of every type of medical and surgical therapy, the doctor-patient relationship is seldom taught in medical schools. The reason for this neglect appears to lie in an emphasis on diagnosis rather than on pathogenesis and treatment. Since it is rather intangible the doctor-patient relationship is usually dismissed as the "art" of medicine, but there are principles even in the practice of an art. To get along with patients one must approach them in the right frame of mind; he must be aware of and try to avoid the slightest sign of annoyance. A raised eyebrow may mean to the patient "Do you mean to tell me that you stayed home from work because of that?" The only safe way to prevent the patient from getting such thoughts is for the doctor to avoid thinking or feeling in that manner while in contact with the patient. The doctor must place himself in the proper frame of mind. If he can put himself in the patient's "shoes" he will realize that irritating symptoms have been developed as a defense against anxiety and that basically the patient is really a fine person. With this realization the doctor will be better able to tolerate irritating actions and caustic comments. If one can consistently assume such an attitude it will become second nature and the patient will automatically and immediately feel that the doctor is truly interested in him. By his thoughts and feelings and by his actions the doctor communicates to the patient. The patient in turn may communicate to the doctor by means of his symptoms and signs as well as by his actions and words.

* A condensation of chapter XIII on Treatment from the book to be published by The Williams & Wilkins Co.

The Time and Expense of Psychotherapy

It is frequently stated that ophthalmologists do not have the time nor can the patient afford to pay for the time necessary for treatment in the form of psychotherapy. Every doctor has seen patients who have gone from doctor to doctor and from clinic to clinic being repeatedly examined, tested, and operated upon but who end up such a routine with complaints similar to the ones with which they started. Of course psychotherapy would not be able to prevent all such cases, but it could help a good percentage of them, and the cost of psychotherapy, although high, is never as high or as wasteful as needless examinations, tests, and surgery. Since ophthalmologists usually work by appointment, they can take the time if they so desire. Some patients may expect to receive extra time without paying anything additional but this should not be allowed. The patient should pay; if he does not value psychotherapy highly enough to be willing to pay for it, he is not a good candidate for treatment. One charges the patient for the time that he has used. If the ophthalmologist customarily charges $5.00 for a 15-minute office call, he has been in the habit of collecting about $20.00 an hour. Thus, if he has spent 30 minutes with the patient he charges him $10.00, and if he has spent 60 minutes he charges him $20.00. Since a doctor becomes more skilled with experience, the ophthalmologist may not want to charge his usual rate while he is learning the technique. He may feel that he should not charge the patient as much as if he were an expert. Such problems of cost to the patient are matters which each doctor must decide, but in any event the doctor *must* feel that the patient is paying his way and that the doctor is not being cheated by the fee he receives. If the ophthalmologist feels that he is not being adequately recompensed, he will be unable to give the patient the warm interest necessary for psychotherapy. On the other hand, if he feels guilty about overcharging the patient, he may fail to be objective in his handling and be too giving and too permissive with the patient.

The Disagreeable Patient

Since patients may be demanding, mean, cantankerous, and non-appreciative, it is of value to understand why they behave in such a manner. The psychotherapist must realize that in all probability the patient does not have a basic dislike of him but that these disagreeable symptoms are methods of defense against inner problems. Levine has pointed out how, in infra-human animals, external dangers result in fear and this in turn gives rise to defenses. The common defenses are freezing, flight, and fight. In our current culture the patient's problem is usually not that of external danger but of a danger which lies within himself. Internal dangers give rise to anxiety which is essentially the same as fear except that the patient does not realize its source. Freezing, flight, and fight are not appropriate reactions to anxiety, so the human organism has developed a series of defenses so numerous and varied that an entire book would be needed to discuss them fully. Such defenses include personality traits and psychosomatic diseases. The personality that the patient presents to the doctor is often less pleasant and appealing than his true or basic personality. The adult may misbehave just as he did when

he was a child when he found that misbehavior helped drain off his feelings and when he found that such behavior got him attention if it did not bring him love.

Transference Reactions

The term transference refers to the repetition of unconscious emotional attitudes that a person had for someone in his childhood directed toward a new person (the therapist) who enters his life. Thus the patient can transfer to the doctor the feelings and attitudes he once had for his father or for his mother. The term positive transference is used when these feelings are of a positive character such as love and respect and the term negative transference when these feelings are of a negative character such as hate.

POSITIVE TRANSFERENCE. Some patients invest a doctor with supernatural power; to these patients, the doctor is a representative of God as once the priest-doctors were supposed to be. Such an aura of mysticism is enhanced by the atmosphere of the doctor's office, where the patient is awed by the equipment which he can not understand. The patient may feel that the doctor has secret and powerful knowledge, just as he once considered his parents to be all-wise and all-powerful. To a degree, such an attitude is a normal and a valuable phenomenon for when a patient becomes ill it is natural and healthful for him to regress to a certain degree to allow the doctor to take care of him. If the patient is able to regress to a childhood level it is easier for him to submit to procedures and follow the advice of the doctor.

NEGATIVE TRANSFERENCE. The patient may react with hostility to the kindest efforts of the physician. When such reactions are out of all proportion to the reason for such behavior, one can safely assume that the mechanism of negative transference is at play. If the ophthalmologist has a patient who behaves as did the following woman, he must realize that she is behaving in such a way, not because she is mean and despicable, but because of a psychologic mechanism of which she is unconscious and over which she has little or no control. If he can truly understand this process the ophthalmologist can avoid feeling hurt when it happens.

Case report. (Landa.) A highly intelligent woman, aged 45 years, asked her dentist to refer her to an oculist for the treatment of an acute eye condition. After her visit, the patient was perturbed and informed the dentist that she felt that the ophthalmologist was not competent. The dentist reassured her and advised her to complete the treatment. Later, the patient remarked that she had decided not to get the new glasses which had been prescribed, because she felt certain that she would not be able to wear them.

She described her first visit to the ophthalmologist in the following way:

"While sitting in the reception room, I could hear the doctor's voice as he received and dismissed patients. I become restless and could not concentrate on my reading. After a while, I became 'boiling mad,' but this lasted only a few seconds. When I finally saw the doctor my resentment became intense again. Everything he said and did irritated me very much."

The most revealing point, which the patient in no way connected with her reaction, was her discovery that the aunt of the ophthalmologist had been her

governess when she was a child. She had feared and hated this governess and had submitted to her discipline only upon the insistence of her father. This patient was reexperiencing her childhood hostility toward her governess; she unconsciously transferred these feelings to the oculist who strikingly resembled his aunt. Although she developed negative transference to the ophthalmologist she continued her positive transference to her dentist and despite her own wishes she continued with the ophthalmic treatment because of this positive transference to the dentist.

False negative transference. The ophthalmologist must beware of assuming that any irritation that a patient shows is transferred to him from an unloving parent. Many of the irritations that a patient displays are due to irritating features in the personality or in the actions of the physician. An example is the anger that most patients experience when a physician keeps them waiting for a couple of hours. Such patients may be afraid to show such anger because of inhibitions or fear that it will disturb their dependent relationship with the doctor, but in any event their anger is there under the surface where it will remain to disturb the doctor-patient relationship.

Counter transference. Counter transference refers to the feelings the physician develops for the patient as a result of his own past experiences. These feelings may be those of love or hate and do not depend on who the person is and how that person behaves but of whom that patient unconsciously reminds him.

In spite of his best efforts the physician may be unable to develop a warm interest in the patient and may even dislike him. In such a case, he must not undertake to do psychotherapy because the most important ingredient of such therapy for the ophthalmologist is the development of a warm interest. If, instead of a warm interest, the doctor develops an active dislike, he can not help the patient. In such an instance he ought to transfer him to someone who can help. An example is senile macular degeneration, a common condition which is becoming more frequent with the increase in life span. These patients can be helped by the doctor's taking a warm interest in them. The patient should not be told that the doctor can not help him unless the physician feels that way. It is true that one can do little or nothing for the organic aspects of senile macular degeneration but he can utilize aids for subnormal vision, and he can apply the milk of human kindness. If the doctor's personality is such that he finds it impossible to ask the patient to return at regular intervals for a little chat, then he should refer the patient to someone who can. If, on the other hand, he believes that he can help the patient the physician should say so since his optimism is a powerful therapeutic tool.

It must not be implied that the ophthalmologist must always spread sweetness and light regardless of the patient's behavior. Patients will often take advantage of a doctor. A doctor's angry feelings are not always preventable or unjustified; limits must be set on the behavior of patients just as they must be set on the actions of children—a happy medium between complete freedom and strict control is desirable.

If the doctor is ill at ease, he will not be able to get his patient to discuss his problems, for the patient will sense this attitude and be unable to speak of his trouble even though he had planned to do so previously.

The doctor will also have to be relatively free from personal conflicts, rigidities of manner, emotional blind spots, and settled convictions as to how people should properly behave. It might be said that any physician who attempts to do psychotherapy with his patient and does not find his patient improving after several months should confer with or refer his patient to a psychiatrist so that he may receive adequate help.

It is possible that the success or failure of interviewing lies as much in the doctor's attitude as in the questions he asks. If the doctor is jittery because other patients are waiting, he can not relax and expect the patient to unwind. The patient will be able to sense the doctor's impatience. It is best to obtain information regarding emotional factors naturally at the time when a history of the illness is obtained, and even an ophthalmologist can make his opening question "Tell me about yourself" or "What is your trouble?" If the ophthalmologist can then relax, the patient may open up with a discussion that leads to his trouble, and he may ventilate much of the conflict seething within him. If the doctor watches the patient closely, he will notice changes in posture or direction of gaze, variations in the inflection of the voice, and in muscles of the face. By such observation the ophthalmologist may note the accentuation of certain facts and the slighting of other material. Thus, if the patient tenses and avoids discussion of a certain subject such as his wife, the doctor can be sure he has found a tender spot. Although the patient may try to be helpful, he may keep such data in repression or, at least, out of his mind. At such a time the physician should draw out the patient and encourage him to discuss such troubling conditions by comments as "Please tell me a little more about your wife." The patient wants to be helped and with encouragement may be able to go ahead and describe his problems.

The ophthalmologist does not often take a long history and he does not have the time available for such drawing out of the patient. If he has a patient in whom he feels that emotional factors are important he should have the patient return for further interrogation. He can say, "That is all the time we have for today. I would like to see you again when we can go into the matter in more detail." When the patient returns, the ophthalmologist can begin the history once again and have the patient amplify the previous data. Since relationships with those who are most important to us cause us the most trouble when they go wrong, the physician can concentrate his history-taking on the immediate family. For example, when the patient has returned for his second visit, the doctor can ask "Tell me how you were feeling at the time this trouble started." If the man happens to mention his wife, the ophthalmologist can add "Could you tell me a little more about her?" There is no need to apologize for such questions or to make any preliminary explanation of why such questions are necessary. When the patient returns for this second visit the ophthalmologist should have from 15 to 60 minutes set aside for seeing him. If at all possible he should avoid interruptions of any type. The patient should be able to sense that the doctor has the time and interest in him and wants him to talk. Obviously the ophthalmologist can not feel relaxed and interested unless he has arranged for the necessary time. Ophthalmologists frequently state that they are too busy or can not afford to take such time with the patient. Since an ophthalmologist usually works by appointment, he can

arrange to take enough time, at least on his subsequent visits. It is much more interesting and rewarding to help a person with a problem than to squeeze in one or two more routine refractions.

PSYCHOTHERAPY

Selection of the Patient for Psychotherapy

The patient should want help and be able to be helped, and the doctor should want and be able to help him.

CRITERIA FOR THE PATIENT. *Diagnosis.* Psychiatrists have found that those cases which respond best to psychotherapy are the behavior disturbances which are due to current stress. The anxiety states respond reasonably well if they have not become extensively organized, but psychosomatic conditions are usually most difficult. Thus, it is often difficult for the patient with uveitis to see the need for exploring and helping his psyche. Even when we succeed in pointing out to him how increased responsibility has helped to bring on his inflammation, he may prefer purely somatic therapy to any probing into his life.

Motivation. Some patients do not wish to get well, because of the marked secondary gain which they receive from the illness; if they were to recover, it might mean giving up their revenge upon relatives whom they feel are responsible for their difficulties. Other patients do not want to lose their disease, such as uveitis, because it would mean giving up their main basis of relationship to others; they would have to give up the attention they receive from the doctors and nurses who take care of them and from relatives and friends who dote on them. Some patients have become demoralized in their long struggle with difficulties and they are no longer willing to face the pain which difficult readjustment evokes. Other patients have never shown a sound capacity to relate themselves to others; they rarely do well under psychotherapy. The willingness to undergo psychotherapy for a large number of people is not so much the desire for recovery as the desire to find someone to whom they can relate. The lonely widow may come to use the doctor as a substitute for her social world. Such a patient will tell her doctor of her minor triumphs and frustrations just as she would have told an intimate friend or her deceased husband; any attempt on the part of the doctor to have such a patient give up her discussion of such a nature for the more traumatic consideration of her major problems will be met by resistance. With dexterity the doctor should be able to use the patient's needs along this line as an incentive to get her to work on her real problems. The ophthalmologist who does not wish to probe into the matter should realize that to allow such a person to come in to chat is to perform a form of psychotherapy which is of definite help.

Current situation. If there is stress which may be relieved by manipulation of the environment, the outlook is good. It may be wise to urge a patient to change from a job requiring daily decisions to one in which the day-to-day requirements are simple. I have seen a uveitis patient who needed constant adrenocorticoid hormone therapy improve dramatically and no longer need the medication only after he had changed to a job with less responsibility.

Intelligence. The less the intelligence of the patient, the more one must rely upon the simple forms of psychotherapy.

Age. As in the case of intelligence, the age of the patient determines the kind of psychotherapy rather than whether or not it should be attempted. The less plastic older individuals are best treated by social measures. This means they should be given new supportive settings that provide an outlet for their creative capacities.

Duration. With the passage of time a symptom may acquire additional meanings. Thus a disease such as uveitis may allow a patient to avoid work and demand increased attention. Since a disease will develop such additional meanings with the passage of time, it is easy to see why the older a condition, the more fixed it becomes, and thus the more difficult it is to cure.

Previous treatment. Previous medical treatment tends to make the patient more resistant to psychotherapy. One reason for this is the way the patient's illness has been interpreted to him by previous physicians. Patients with anxiety neurosis, who have been given organic interpretations of their illness, are always difficult to treat. Cameron has found it useful to undertake a period of instruction about how our bodies work.

CRITERIA FOR THE DOCTOR. If the ophthalmologist believes that he can not help a patient, he ought to say so and transfer the patient to someone who can; but if he believes that he can be of help, he ought to tell him so. Whether the doctor can help the patient will depend upon whether he likes the person and feels capable of helping him. It would be foolish to undertake major psychotherapy without proper training, just as it would be foolish to undertake major surgery. Most physicians are capable of doing minor psychotherapy just as they are capable of minor surgery, but in either case it helps to gain as wide a background as possible. In addition to extensive reading it is urged that the doctor attend classes and seminars arranged for residents in psychiatry and that he treat several patients under the supervision of a psychiatrist.

A psychotherapist must be able to sit quietly and listen to the patient's complaints and follow the thread of his associations in order to discern the central problem; he must be able to use words that will relieve the patient's anxiety and support him in learning to deal with his problems. Since capacities vary from doctor to doctor, one should attempt to do only that which he is interested in and capable of doing.

THE REFERRAL OF A PATIENT TO A PSYCHIATRIST. In this day of specialization, few physicians can be skilled in handling both somatic and psychologic aspects of diagnosis and therapy. Since it takes most of a lifetime to learn the basic assumptions as well as the necessary therapeutic procedures in any one field—not to mention the time and effort involved in keeping up with the rapid rate of progress—the practitioner would have to be a dual specialist. It may be best to teach the ophthalmologist the basic methods of psychiatry so that he may learn the procedures necessary to diagnose a significant emotional factor and understand its potentialities. Many of the leaders in the psychosomatic movement are convinced that the non-psychiatrist should not attempt psychotherapy but should understand its place and be able to see that the patient is referred for its execution.

How to decide whether or not to refer the patient. If the patient appears to be ill enough and to offer some hope of improvement, referral to a psychiatrist should

be considered. It is often wise to have a division of labor; the ophthalmologist may continue the medical treatment while the psychiatrist undertakes the psychotherapy. If he is interested and feels capable, and if the goals are limited, the ophthalmologist may undertake both aspects of the case, but he should do so under the supervision of a psychiatrist. If the disorder is mainly psychiatric (such as severe asthenopia without any abnormal ophthalmologic findings), it may be wiser to have the psychiatrist assume full charge. In such patients it is usually best not to complicate matters with somatic treatment. On the other hand, it is sometimes wisest for the ophthalmologist to maintain control of the patient and utilize the psychiatrist simply as a consultant. In such an instance the ophthalmologist may ask advice of the psychiatrist or the psychiatrist may see the patient one, two, or three times and then refer the patient back to the ophthalmologist. Such a procedure may be the best one in those cases in which the patient has a good working relationship with the ophthalmologist, does not care to be treated by a psychiatrist, and can be handled by the eye specialist.

The type, quality, and availability of psychiatrists is important. It is difficult enough to get a patient to a psychiatrist in the same building; if the patient has to travel a long distance he will be much less interested. The ophthalmologist will, of course, refer patients whom he believes are suicidal or homicidal or who can not be taken care of outside of a psychiatric hospital. As elsewhere in medicine, it is usually wise to avoid a radical program of treatment if more conservative measures will suffice. Once the ophthalmologist has decided to refer his patient to a psychiatrist, he must begin to prepare him.

How to prepare the patient for the referral. The patient must be shown that emotional factors are involved in his illness; in doing this the role of somatic factors should be de-emphasized. To demonstrate how such a referral might be accomplished let us consider the case of a young woman who developed a chorioretinitis after arriving home from the hospital where she had delivered her third child. Unfortunately her husband was forced to leave town at this critical time. The etiologic workup for uveitis revealed a probable diagnosis of toxoplasmosis. The referral to the psychiatrist was accomplished in the following way. "We have found that the inflammation in your eye is due to a parasite which produces the disease known as toxoplasmosis, but toxoplasmosis is a common condition. Apparently about one-third of all people your age have or have had the disease. There must be other reasons why your eye became inflamed. You will remember that it got bad just after you got back from the hospital with your third baby and your husband had to leave town, leaving you with extra work and extra responsibility. We have seen that extra responsibility frequently helps bring on such an attack; we have had three patients lately whose eye trouble started with the responsibility and worry of buying a new home. As you probably know, in medicine we are finding that emotional factors help cause many different diseases. Even the common cold, which is due to a virus, may be precipitated by an emotional upset. For these reasons I feel that it would be wise to go into such factors in your case. I know that if I had such an inflammation I would have my emotional life investigated to see if any help could be obtained along that line; one

wants to do everything possible to save his eyesight. I would recommend that you see Dr. "H", who is especially interested in patients with your problem. Let's get his opinion to see if he can be of help. He is a psychiatrist and the one best able to determine if emotional factors are important in your case. He will see you about three times to get a complete history. After that a decision can be reached as to how important emotions are in your case and whether you should have any further treatment from Dr. "H"."

I think it is wise to call the psychiatrist a psychiatrist and not camouflage him, because the patient will find out later and may have a severe reaction to the attempt at deception. It is best to be honest with patients. In some cases when I feel it is needed, I explain that a psychiatrist's job is not just with crazy people but is mainly with normal people who are having troubles with their feelings and emotions; he is a specialist in such things and the one best prepared to give assistance. With such an explanation, I have found that over 75 per cent of uveitis patients will accept the referral to a psychiatrist. Even those who do not complete treatment may be helped, because the history which is taken helps point up to them how they can help themselves. If the relations between the onset or exacerbation of a condition and external events can be pointed out to the patient, he is more easily convinced of their importance. To do so it is necessary for the ophthalmologist to take a history and make such connections. It is obviously much less effective to tell a patient, "You have uveitis, therefore you should see a psychiatrist." Many patients resist referral. Instead of getting angry, the ophthalmologist must try to understand their feelings and try to continue his gentle investigation of their emotional life and his psychologic support. He should not reject them because they have failed to take his advice; they have failed mainly because of fear of what they may find within themselves. Usually, the sicker the patient, psychiatrically speaking, the more he will resist referral. Such a patient needs support, and if the ophthalmologist can give out with a warm interest, he will be doing a great deal to help at a time when support is sorely needed.

Advice for Beginners

Although all doctors can not avoid practicing psychotherapy in some form, it is the most difficult branch of medicine if one attempts to learn all there is known about the subject and becomes expert in its application. I say this since it is necessary to take an additional 3 to 5 years of training after one has become a psychiatrist if he wishes to become certified as a psychoanalyst. Psychotherapy is surgery of the mind, although the anatomy of the mind demonstrates tremendous individual variations. Thus the psychotherapist who attempts surgery on the mind must be constantly alert in order to be oriented as to where he is at any one moment. Any physician feels competent to perform surgery on the scalp; it is when a hole is made in the cranium that special skills are needed, but even scalp surgery takes some knowledge and caution and it is in this vein that the following words of advice are given to the beginner in psychotherapy.

1. Relax and be friendly.
2. Keep your mouth shut; let the patient do the talking.

3. If you do say anything, couch it in subtle terms.

4. If the patient asks too many questions or asks for too much advice, avoid these questions by comments such as, "Why did you ask?" or "Could you explain a little more what you mean?" The reason for the patient's questions may be that it is difficult for him to reveal his feelings so he appeals to the ophthalmologist for interpretation, advice, and prescription, desiring anything which will protect him from the painful process of self-revelation. If he suspects that the feelings are too much for the patient to tolerate, the ophthalmologist should change the subject temporarily. In the average case, however, he should encourage the patient to continue by telling him gently that it is premature to attempt solutions at this stage. The physician can demonstrate his interest and warmth by saying, "I'd like to know a few more details" or "It would help if you could tell me more about your feelings." He must not fix the patient with a critical stare. If the ophthalmologist is uncritical and accepting, the patient is reassured so that the revealing of his inner thoughts is made less painful.

5. Learn all you can about psychodynamics. A naturally humanitarian attitude and an interest in people have always been considered to be important features of a good doctor, but we are now coming to realize that it is also desirable for the doctor to have a penetrating knowledge of psychology and an interest in what makes people behave as they do. The patients seen by physicians have changed in type; fifty years ago trachoma and gonorrheal ophthalmia were common and there were fewer patients who reached a ripe old age, while today the hospitals are filled with patients with stress diseases. The modern physician should be able to detect evidence of strain in patients who are apparently well adjusted and are totally unaware of serious emotional problems (Wolf); he needs to know as much about emotions as he does about drugs or microbes.

How Long and How Often to See the Patient

The depth of psychotherapy will be determined in part by the frequency of the interviews. Thus in psychoanalysis the patient is seen almost daily. The patient soon runs out of current events and current complaints to discuss and is led back into a consideration of his past life. The ophthalmologist should avoid any extensive investigation of the patient's past life and should concentrate on more superficial and current aspects. One way to avoid the danger of too deep penetration is to have the patient return for interviews no more frequently than every week. When it is desirable to pull the patient back from too deep a penetration of his problems (for the ophthalmologist to handle) and when it is desirable to terminate the patient-therapist relationship at the conclusion of psychotherapy, the intervals between psychotherapy should be lengthened with the consent of the patient. When terminating treatment, the physician can first increase the time to two and then to three and four weeks and end up with telling the patient that he need not come back unless he feels the need. The patient should leave psychotherapy with the feeling that the doctor will always be there and willing to help him; this knowledge helps support him as he faces the world again on his own.

The amount of time that should be spent at each interview can be based on similar principles. It is seldom advisable to spend more than one hour with a patient except, perhaps, for the early diagnostic work-up. Except for the most superficial type of support in which the doctor simply chats with the patient, I feel that 20 minutes is a minimum period needed; 60 minutes should be the maximum. The ophthalmologist thus has some latitude and he can adjust the time to best suit him and his patient's needs. It would probably be best in the average case to start with a period of 30 minutes and adjust this time if it seems indicated.

As every physician has discovered, once a patient has begun to talk he frequently is difficult to stop. The psychotherapist must be firm in this regard; the patient should be instructed beforehand that he will have just so much time and when that time is up, the doctor can rise from his desk if necessary to indicate that the session has ended. Usually all that is necessary is to state simply; "That's all our time for today. How will eleven o'clock on the same day next week be?"

Whether psychotherapy should be continued for a few weeks or a few years will depend upon the situation in each individual case. If the patient is making progress and both he and the doctor desire to continue, it should be all right to do so. It is never possible to predict in advance just how long psychotherapy will take. Frequently the patient decides when he has had all the help he needs, and he will terminate treatment himself. At other times the doctor should terminate treatment because the patient is not making full use of the time. If the psychotherapist does stop therapy he must do it gently and not impart a feeling of rejection to the patient.

Clinical Practice

ANESTHESIA AND SURGICAL TECHNIQUES

ANESTHETICS AND RELAXANTS IN OPHTHALMIC SURGERY

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In discussing the use of anesthetics in ophthalmic surgery, Nigel Cridland (Portsmouth) dealt primarily with operations for cataract extraction because if anesthesia is adequate and safe here, it is likely to be so in all ophthalmic surgical procedures. Anesthesia has many advantages over analgesia. The intraocular tension is appreciably reduced and can be reduced further by a posture which the conscious patient would find uncomfortable. The natural position of the eye is such that although he always places a suture in the superior rectus, it is but rarely used for traction. Under anesthesia, the position of the eye approximates to the primary position rather than to that of Bell's phenomenon. The return of ocular movement may, perhaps, occur later than under analgesia, but the advantage to wound healing of the longer immobility is obvious. Even more advantageous is the fact that the return of sensation to the eye is roughly cotemporaneous with the return of consciousness; in analgesia it is delayed, and the postoperative composure of the patient is again disturbed, be it ever so slightly, by returning sensation.

Other more obvious advantages of anesthesia are (1) complete removal of the patient's anxiety and of the need for his cooperation; (2) the surgeon's freedom to concentrate on the operation instead of having to attend to both operation and patient, with a consequent reduction of mental tension; (3) ability to operate more leisurely (4) absence of swelling of the lids; and (5) absence of proptosis, and elimination of retrobulbar hemorrhage which sometimes compels postponement of the operation.

The disadvantages of anesthesia also deserve consideration. The risk to life has been greatly reduced and need not now be regarded as disproportionate. The risk of complications, chiefly respiratory, must be accepted, but the danger of these also has been substantially reduced. The recovery period from anesthesia calls for more concentration of nursing care in the immediate postoperative period; by the second postoperative day, however, there is little to choose between anesthesia and analgesia as regards the general physical well-being of the patients. Coughing can be almost entirely avoided by forethought on the part of the anesthetist and, to a large extent, so can postoperative vomiting. Other violent expulsive spasms, such as retching and sneezing, are less easy to control, but their effect on the eye can be almost nullified by the use of the Williamson-Noble suture.

The value of anesthesia in cataract extraction has been assessed in 157 patients who can fairly be regarded as a representative sample of the cararact popuulation in relation both to age and the quality and quantity of prior diseases. Analysis of the results in this series lends little support to the superficially reason-

able expectation that complications or difficulties are more apt to arise in patients with antecedent disease. Difficulties or complications attributable to anesthesia occurred in 12 cases out of the 157, a proportion of 7.6 per cent. In three, they were ocular in character (anterior synechia in two and late iris prolapse in one). The general postoperative complications consisted of respiratory disturbances, which were severe in two patients and mild in four others; transient restlessness and disorientation in three patients 77 years of age or over; and vomiting in one. The good results obtained in this series seem to show that anesthesia in cataract extraction is not inferior to analgesia in respect to either operative difficulties or postoperative complications.

H. B. C. Sandiford (Portsmouth) stated that the anesthetist's approach to ophthalmic surgery should be the same as his approach to surgery in infants and young children. Both are highly specialized and require operative conditions that are not needed for general surgery. The operative conditions at which he aims are a nearly bloodless field, with a low intraocular tension in a fixed eye for lens extractions, and, above all, a smooth recovery without coughing or vomiting. While these conditions may not yet be obtainable in every case, the good results now being secured by modern techniques hold out hope for the future. It should be noted, however, that anesthetists who specialize in ophthalmic surgery have studied the subject and make it all look easy. There is a real danger that when the usual anesthetist is absent the patients will be anesthetized by one who is not familiar with the work and that the results will therefore be indifferent or even bad.

Turning to the use of relaxants, A. B. Nutt (Sheffield) said that after 15 months' experience with largactil (Chlorpromazine) given intravenously for intraocular surgery, he felt that it had three outstanding advantages: (1) There is no need for anxiety about the behavior of the patient and the operation can thus be carried out carefully and without hurry; (2) the risk of complications during and after operation is reduced to a minimum; and (3) the patient is free from apprehension during the operation and sleeps peacefully for some hours afterwards, allowing an initial period of very quiet convalescence.

H. L. Wilson described the use of chlorpromazine hydrochloride in over 100 patients, three-quarters of whom had cataract and the rest glaucoma or conditions requiring corneal grafting. The results were consistently good. J. J. Healy (Llanelly) discussed the advantages of local anesthesia and R. A. Burn (London) reported on the results obtained in 143 patients with a combination of chlorpromazine, phenergan, and pethidine (a barbiturate). This combination was especially valuable because of its ability to eliminate apprehension and the tenseness that goes with it.

Finally, C. H. Bamford said that he had used curare in 88 patients undergoing cataract extraction. In 86 the effect was good, but one patient became restless and cyanosed during the operation, probably because the curare was given too quickly. She recovered and the operation was satisfactorily completed. After this experience, the second in the series, the drug was always given very slowly. The last patient, however, also became restless and although the operation was completed successfully, the respiratory difficulties encountered in this case were so severe that the use of curare has been given up completely.

Comment: Great progress has been made in anesthesiology in the past 15 years, and now it would appear that a critical analysis of techniques in regard to anesthesia for ophthalmic surgery is in order. The need for such an analysis is shown by the papers comprising this discussion since the only things which these five ophthalmologists and two anesthesiologists can agree about is that there should be no coughing or retching during or after intraocular surgery, and that it is imperative to have a team of a good anesthetist and an ophthalmic surgeon who are accustomed to working together. No one can possibly disagree with these two principles, although one might argue with some of the techniques employed to achieve the first of these two aims.

Although Mr. Cridland clearly enumerates the advantages of general anesthesia over local "analgesia," the incidence of 7.6 per cent complications which he attributes to complications of general anesthesia, seems unduly high. I know of no series of cataract extractions which has been analyzed in a way to show what percentage of complications might be due to faulty anesthesia, but personal experience leads me to doubt that it would be 7 per cent.

Some of the methods described might be applicable in certain teaching centers, but by and large, ophthalmic surgeons will be well advised to stick to local anesthesia combined with judicious sedation until such time as the techniques of general anesthesia are more advanced than they are at the present time.

DANIEL SNYDACKER

THE EFFECT OF RETROBULBAR ANESTHESIA ON INTRAOCULAR PRESSURE

D. P. GREAVES

London, England

Trans. Ophth. Soc. U.K., 1955, *75:* 121–135

The possibility that, in addition to affecting the tone of the extraocular muscles, a retrobulbar anesthetic might influence the blood supply to the eye either by by direct action upon the blood vessels or by interfering with their nervous control led the author to undertake a comparison of clinical and experimental results. The anesthetics used in the clinical studies were 2 per cent xylocaine with adrenaline 1:80,000; 4 per cent procaine; and 4 per cent procaine with adrenaline 1:20,000. Hyaluronidase was added in some instances at the rate of 150 units per cubic centimeter.

Tensions were taken with a Schiötz tonometer immediately before operation, the patients being taken from those admitted for the treatment of cataract and glaucoma. All were given phenobarbitone, 2 gr., 1¼ hours before operation, and in each case the patient was allowed to lie on the operating table for five minutes before the first reading was made. Patients with cataract received instillations of 2 per cent homatropine HBr and 2 per cent cocaine HCl, in the ward, and those

with glaucoma were given amethocaine drops in the operating room. Those with cataract were then given a facial injection of xylocaine and adrenaline, and a second tension reading was taken five minutes later. The retrobulbar injection was given through the conjunctiva of the outer part of the lower fornix with the the patient looking up and slightly inwards. The needle was inserted for not more than 3 cm. aiming between the inferior and external rectus muscles. The injection would thus be given just behind the globe in order to avoid a retrobulbar hemorrhage, which is very much more likely to occur if the injection is given into the apex of the muscle cone. A reading was taken five minutes later and again at the end of another five minutes. Patients with glaucoma were treated in the same way except that the facial nerve was not injected. The degree of paralysis of the extraocular muscles was assessed according to Gifford's system, counting 20 per cent for each rectus and 10 per cent for each oblique muscle paralyzed, the movement being checked after the last tension reading. The percentage drop in tension due to the retrobulbar anesthetic refers to the maximum fall produced by the latter alone and is taken from the level reached five minutes after the facial injection.

Analysis of the results obtained in patients with cataract shows that facial akinesia itself produced a definite lowering of tension in all but one of the nine cases studied, the mean percentage drop being about 13 per cent. The retrobulbar injection produced a further fall in all nine patients, the maximum effect being reached in most cases about five minutes after the injection. An interesting feature was the apparent absence of any correlation between the degree of muscle paralysis and the fall in pressure. Three eyes showed a marked lowering apparently without any degree of ocular muscle palsy. Furthermore, the addition of hyalase in several instances did not seem to have any extra tension-lowering effect. The only result with procaine alone showed rather less of a fall than that recorded in most of the other cases, in spite of pronounced muscle paralysis. Some risk may accompany the use of a retrobulbar anesthetic in hypertensive patients. One such patient showed a rise in pressure during the second five-minute period following the retrobulbar injection and his maximum percentage drop was only 8 in spite of a 20 per cent muscle paralysis. No clinical evidence of hemorrhage into the orbit was seen, but immediately after the section had been made, it became evident that there was a postive vitreous pressure greater than usual. A complete iridectomy was performed, the lens being left undisturbed, and the eye healed well. Later examination, however, showed that a moderately large choroidal hemorrhage had occurred in the lower half of the fundus. This course of events may have been related to a release of marked vasoconstrictor tone in a hypertensive patient with spastic and not organic changes in the peripheral arteries.

In all but 1 of the 5 patients with open-angle glaucoma, the maximum fall occurred at the end of the first five minutes. In three eyes there was a rise of intraocular pressure during the second five-minute period; all three of these had had hyaluronidase with the anesthetic. A similar rise was also seen in one of the patients with narrow-angle glaucoma; he, too, had had hyaluronidase. Again, no

correlation between the degree of muscle paralysis and the amount of reduction in intraocular pressure was discernible in these patients, in most of whom akinesia of the extraocular muscles was moderate or slight. If the method of assessing muscle tone reduction is reliable, some extra mechanism must have been contributing to the lowering of tension. The possibility that this additional factor might have to do with the neurovascular system suggested an experimental approach.

Rabbits anesthetized with intravenous urethane were used as experimental animals, and continuous blood pressure and intraocular pressure recordings were made after retrobulbar injections of various anesthetics. The experimental results, taken in conjunction with those obtained in the clinical cases, show that a retrobulbar anesthetic produces a change in intraocular pressure by its action on vessels in addition to that caused by an alteration in extraocular muscle tone. Whereas in the rabbit vasoconstrictor tone appears to predominate, it seems probable that vasodilator tone is largely present in man except when peripheral vasoconstriction exists as in hypertension.

Comment: The work done on humans substantiates that done by other investigators on the tension-reducing effect of retrobulbar anesthesia. The fact that the author found a reduction in intraocular tension following a Van Lint akinesia averaging 13 per cent is difficult to understand. This reviewer knows of no substantiating work. On the face of it, a reduction of tension would scarcely be expected in all cases since there is such a great difference in muscle tonus of the orbicularis oculi muscle in different individuals; an effect on tension in an elderly individual with very lax lids would not be expected.

The animal experiments are very interesting but the findings are difficult to explain. The author's suggestion, that there is a release of sympathetic tonus, seems likely. Certainly both in humans and in animals, such changes in pressure as occur are related to changes in blood flow, but the fact remains that not a great deal is known concerning vascular innervation and the effect of various agents on this nerve supply.

DANIEL SNYDACKER

THE USE OF AIR IN EYE SURGERY

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Tr. Ophth. Soc. U. Kingdom, 1955, *75:* 33–41

The value of the intraocular injection of air as a therapeutic measure or a diagnostic aid (except in cases of a fissured orbital fracture involving an accessory nasal sinus) may be questioned, but its usefulness in the field of anatomic restoration and replacement deserves consideration. It may also prove advantageous when used in the anterior chamber to give greater room for instrumental

maneuvering and to render the anterior synechiae more taut and so make them easier to divide. Similarly, it may be of some value in the maintenance of fistulous tracts made in glaucoma operations and in exerting intraocular pressure for a time against the vitreous and retina after retinal detachment operations.

The relative safety of air injections into the eye probably depends on its physical properties. It forms an elastic, readily compressible cushion, and the place it occupies in the eye may be to a great extent controlled by the position of the patient. For these and other reasons, it has advantages over a saline solution, which dilutes the intraocular fluids and is noncompressible and space occupying.

Bacterial investigations on specimens of operating room air drawn (1) through a cotton filter, (2) a spirit flame, and (3) through heated needles showed no bacterial growth after 72 hours by these three different methods of sterilization. The author's preference is for a 2 ml. all-glass syringe which has been autoclaved with its plunger withdrawn to its full extent and so far, after 10 years' routine use of air for cataract, corneal grafts, retinal detachment, and some glaucoma operations, there have been no instances of infection.

Although air embolism has been observed to follow the injection of air into the eye and orbit of an experimental animal, no instance of this general complication has been recorded in human beings. Air glaucoma, though rare, is a possibility. According to Duke-Elder, the way to avoid this danger in clinical surgery is to inject a large bubble of air. If the air bubble is of such a size that it cannot get through the pupil, the procedure is safe, because the cohesion due to surface tension will keep the bubble from subdividing. If air is injected at too great a pressure at the end of a cyclodialysis operation, it may cause herniation and rupture of the pars plana in the incision with vitreous loss. Such a catastrophe is unlikely to occur when the incision is made radially at the limbus as in Allen's modification of cyclodialysis.

The five common conditions for which air may be used at the end of operation to effect either anatomic restoration of the anterior chamber or replacement of intraocular membranes are cataract, glaucoma, retinal detachment, those requiring a corneal transplant, and those in which synechiotomy is indicated. The value of air injected at the end of a cataract operation is that it separates the iris and vitreous face from the cornea and the sutured section; it restores a collapsed cornea to its normal curve, and undoubtedly assists the early reformation of the anterior chamber. The injection should be made when the section sutures have been tied, the superior rectus stitch removed, and all lid retraction devices taken away except one suture just above the center of the lid margin by which the assistant can gently hold the lid upwards away from the eye to expose the whole cornea.

Air injected into the anterior chamber in cyclodialysis operations for glaucoma should fulfill a threefold purpose: (1) it should check hyphema; (2) it should widen and keep open the intraocular fistulous tract between the filtration angle and the suprachoroidal lymph space; and (3) it should re-form the anterior chamber. In patients with retinal detachment, the drainage of the inter-retinal fluid through the diathermy penetrations is greatly helped by the injection of

sterile air into the vitreous chamber. Air injections, however, should not be used in the case of large retinal tears or when drainage has been made through a trephine hole. At the end of a corneal transplant operation, air may be used to restore the anterior chamber and to prevent anterior synechiae from jeopardizing the transparency of the graft. In synechiotomy, after division of anterior and peripheral synechiae, sterile air may well be injected into the anterior chamber to keep the raw surfaces of the iris and the cornea separated until the anterior chamber is well established.

After operation, as the air injected into the eye rises, the patient's head is placed so that the air bubble may separate the structures it is intended to keep apart, or, in the case of retinal detachment, so that it can act to press the retina against the choroid at the site of the tear.

Comment: There are certain disadvantages to the injection of air into the anterior chamber following cataract extraction and glaucoma procedures which have caused many men to abandon this practice. The main disadvantage is the fact that the air may get behind the iris following cataract extraction, and most surgeons would be reluctant to turn the patient upside down and shake him as Cecil O'Brien advocated. Moreover, with corneoscleral sutures and adequate closure of the wound, it is questionable whether air injection serves any real purpose. In glaucoma procedures, even stronger exception might be taken to the procedure. The success of any filtering procedure depends on early and adequate flow of aqueous through the fistula. Although air put into the anterior chamber may cause the iris-lens diaphragm to fall back, it also acts as a dam, preventing the flow of aqueous through the wound, and so might actually defeat the purpose of the surgery.

The use of air injected into the vitreous cavity following detachment surgery has two main contraindications. One is the fact that the fundus is not visible so long as the air remains, and thus no opinion can be had as to whether the retina is flat or not. Secondly, the wisdom of further destroying or distorting an already abnormal vitreous might be questioned.

On the other hand, injection of air in the presence of an intact iris-lens diaphragm when a corneal transplant has been performed appears to be of real benefit. Even here, one wonders whether the cornea and particularly the graft might not be cut off from nourishment by the air bubble.

Some men advocate the use of air in the anterior chamber in cataract extractions when vitreous has been lost, with the purpose of driving the presenting vitreous back from the wound. This plan might have some merit.

The use of air in securing re-formation of the anterior chamber in cases of delayed restoration of the chamber, coupled with drainage of the subchoroidal fluid would also seem to have merit

DANIEL SNYDACKER

THE CORNEA

CORNEAL PIGMENTATION

JAMES HAMILTON DOGGART

London, England

Tr. Canad. Ophth. Soc., 1954–1955, *7:* 238–246

Large-scale invasion of the cornea by pigment may attract a patient's attention and lead him to seek advice; more often, however, pigmentation of the cornea will be noticed during a routine examination of the eyes by an ophthalmologist. Sometimes the explanation is immediately obvious, as when a foreign particle is implanted on the surface of the cornea. Again, cases that may at first appear baffling can often by explained by reference to the patient's general condition, because pigmentation may accompany certain systemic diseases. No scheme of classification, however complete, will make it possible automatically to recognize the diverse examples of corneal pigmentation that arise in practice; yet there are advantages in classification because with it the most likely reasons for pigmentation in a given case are less apt to be overlooked.

Corneal pigment may be endogenous or exogenous. When endogenous, it may be linked with metabolic disturbance or neoplastic growth; often, however, it is harmless and insignificant. Exogenous pigmentation may be caused by foreign matter introduced as such, or it may be derived from foodstuffs or drugs absorbed through the alimentary canal. Vaporized particles flung off by industrial processes can be absorbed through the lungs, skin, or otherwise, and may later emerge into the cornea, though not necessarily in their original form. They may change color in transit as a result of their chemical affinity for other substances. The attempt to classify cases of corneal pigmentation is not merely an academic exercise, because while pigment in some patients may never give rise to trouble, in others a malignant pigmented neoplasm extending into the cornea will jeopardize life.

Patients who seek advice because they have noticed corneal pigmentation should be asked how long it is since it was first noted, and whether it has increased in extent. Inquiries should also be made about trauma, associated manifestations of disease elsewhere in the body, and previous eye treatment. Age, sex, race, occupation, and places of habitation may also be significant. The clinical examination should include a search for pigmentary disorders or other signs of abnormality in the patient's face. The size, shape, and position of the pigmented region in the cornea as revealed by naked-eye inspection may well be diagrammed, and the existence of abnormal pigment in any of the other outer-eye structures noted. Further details may be gleaned by means of a loupe with focal illumination, and slit-lamp microscopy will show location in depth. In cases in which the

triviality or seriousness of a patch of pigment cannot immediately be determined, temporizing is reasonable. The affected eye should be photographed at intervals and if no change can be seen in the successive photographs, the possibility of a malignant neoplasm is lessened or altogether excluded.

The main expanse of the normal cornea is colorless as viewed in ordinary illumination, although certain color effects are elicited by slit-lamp microscopy. At its extreme periphery, the cornea is normally vascularized over a distance of about 1 mm., and occasionally a fleck of superficial blood-staining may be seen after rupture of a vascular twig. The principal varieties of corneal pigmentation are (1) congenital pigmentation; (2) pigment in scars; (3) adventitious pigment unassociated with ocular or systemic disease; (4) pigmentation associated with corneal dystrophy; (5) exogenous pigment; (6) uveal pigment; (7) pigmentation associated with systemic disease; and (8) neoplasm.

1. *Congenital* pigmentation of the cornea is rare, follows no special pattern, and is usually confined to the limbal region.

2. *Pigment in scars* does not necessarily supply any clue to the etiology of the original lesion. In that form of pigmentation which is apt to arise in any long-standing corneal opacity, whether the original lesion was traumatic or inflammatory, we often find linear yellow or brown pigment in the superficial layers of the opaque area. The exact composition of this coloring matter is not known, nor do we understand its pathological significance. Crystals, which can occur in any kind of long-standing scar, are another possible colored item in the cornea.

3. *Adventitious pigment unassociated with ocular or systemic disease*. Hudson discovered that a similar superficial line of brownish pigment may occur in the cornea of an otherwise normal eye, and without any associated disease elsewhere. Some years later Stahli gave a detailed description of the same phenomenon under slit-lamp microscopy. This brownish line occupies the superficial layers of the cornea for a length of 2 to 10 millimeters in the interpalpebral zone at about the same level as the lower margin of the pupil. It may be straight or undulating and occasionally divaricates. We seldom find it in patients less than thirty years old, and it does not interfere with vision. Its composition and significance are not yet fully understood.

4. *Pigmentation associated with corneal dystrophy*. Around the most salient portion of the cornea we usually find, in cases of keratoconus, a ring of superficial brownish pigment which may be interrupted at one or more parts of its circumference. Although morphologically different, it looks as though its composition were the same as that of Hudson's line and those similar lines which develop in old corneal scars. Conical cornea is usually included in the group of corneal dystrophies, and there is no special liability to pigmentation in the other dystrophies that afflict the human cornea; namely, familial keratitis, marginal degeneration, band-shaped opacity, and Fuch's dystrophy.

5. *Exogenous pigment*. Foreign bodies clinging to the anterior surface of the cornea include metal particles, vegetable fragments, and various other pieces of material. Pieces of iron or steel commonly give rise to a rust ring in the adjacent

zone of the cornea, but all or most of this rust will vanish if the foreign particle is removed without delay. Fragments embedded in the substance of the cornea should as a rule remain undisturbed, because complete removal means a permanent scar. In firework manufacturers and other people busy with gunpowder, we occasionally see multiple pigmented particles in all layers of the corneal substance. The same phenomenon may follow air raid injuries. Fortunately, the cornea seems able to tolerate many foreign substances, and interference with vision may be remarkably slight. Unless the material is chemically injurious, signs of irritability tend to disappear within a few months.

Corneal argyrosis follows upon prolonged use of silver nitrate or of argyrol and other organic silver preparations used as eye drops. A characteristic slate-gray stain is manifest all over the conjunctiva, and slit-lamp examination reveals a gray or greenish-gray tinge of Descemet's membrane at its periphery. Sometimes the deeper layers of the substantia propria display similar tinting together with a curious reticulation. Gold salts, copper, and iron may be deposited with characteristic patterns.

6. *Uveal pigment* may be detected in all the corneal layers of an eye that formerly sustained a perforating wound with prolapsed iris. Inflammatory precipitates glued to the hind surface of the cornea by an attack of anterior uveitis usually gather pigment as time goes on. A few pigmented granules from the posterior layers of the iris are almost invariably to be seen on the back of old people's corneae. In some myopes, pigment is so precociously scattered that innumerable particles cling to the endothelium, and occasionally the thermal currents of the aqueous dispose them with special lavishness upon a spindle-shaped central area. These agglomerations, which are known as *Krukenberg's Spindles*, are occasionally visible with the naked eye, but slit-lamp microscopy will always reveal a multitude of granules besides those that map out the spindle.

7. *Pigmentation associated with systemic disease.* Deposits of pigment in the cornea were detected by Sallmann and Smith in cases of *alkaptonuria*, and it is worth recalling that Osler had previously noted scleral pigmentation in the same disease. Most ophthalmologists are aware that patients suffering from Paget's disease may exhibit angioid streaks in their fundi, but it is often forgotten that in this disease we may also find pigmentary change at or near the level of Bowman's membrane. The Kayser-Fleischer ring is a striking feature in Wilson's disease, and it consists of a golden-brown tint occupying part of the thickness of Descemet's membrane.

8. *Neoplasm.* Benign melanomatous accumulations at the limbus may slightly encroach upon the cornea. Sometimes they become cystic, and then there may be a shift of pigment. Therefore slight alterations in the appearance of these tumors are not necessarily signs of danger. Malignant melanoma of the outer eye usually appears as a widespread melanomatosis, but borderline cases occur from time to time. Perhaps it is best in such circumstances to lean toward conservatism because, even if the doubtful swelling is really a sarcoma, its malignancy may be so intense that no treatment, however drastic, would have availed.

In conclusion, it may be noted that corneal pigmentation has important medicolegal implications because it may supply evidence concerning previous injury to the eye.

Comment: The routine use of the slit-lamp has indicated that corneal pigmentation is much more common than was previously appreciated. Doggart has brought out several points worthy of emphasis. It was common during the war to see soldiers who had received blast injuries whose corneas showed hundreds of minute deeply imbedded particles of foreign matter. These gave rise to surprisingly little irritation and did not interfere with vision as much as their appearance suggested. Despite the temptation to remove them, the eyes did best when they were allowed to remain since their removal was always associated with considerable scarring and decrease in vision. The release of pigment with manipulation of the iris in surgery should be emphasized. Atkinson has described decreased vision following cataract surgery because of uveal pigment adhering to the corneal endothelium in the visual axis. Routine irrigation of the anterior chamber can minimize this complication even though the surgery itself has appeared to be minimally traumatic. We were recently dismayed that following an uncomplicated iridencleisis wherein the iris prolapsed spontaneously into the incision and the anterior chamber was not entered to find much iris pigment on the cornea postoperatively. Now we irrigate the anterior chamber routinely following the incarceration of the iris pillars even though the iris has not been manipulated within the eye.

THERAPEUTIC KERATOPLASTIES

G. P. Sourdille

Tr. Canad. Ophth. Soc., 1954–1955, *7:* 53–56

Nantes, France

The technique of lamellar keratoplasty first published in 1840 by Walters, Muhlbaver, and Königsoffer was used almost exclusively by many surgeons until the second quarter of the 20th century, when it fell into nearly complete discredit. Interest in the procedure was revived about 1946 by the first publications of Louis Paufique. In his work with Paufique, the author became especially interested in the technique of total lamellar grafting. In 1948, the availability of antibiotics, cortisone, and beta therapy made perforating and lamellar keratoplasties much easier to perform and from the optical point of view the results then obtained were almost as good as those recently published by R. Townley Paton. In fact, 27 of 28 such operations performed by various surgeons in Nantes in 1948 were entirely successful.

From the optical point of view, few improvements have been made in recent years in the cure of partial leukomas which reduce vision. Attainment of many of the aims of the biologists, however, has been made possible by the security afforded by lamellar techniques, and many new facts of interest have been

brought to light. In many cases of evolutive Hutchinson's keratitis, the author's use of small cadaveric grafts had the amazing effect of stopping the penetration of vessels into the cornea even though it had already begun. Possibly, the presence of one or more antivascular substances in healthy corneal tissue may explain the lack of any vessels in the cornea under physiologic conditions. Moreover, penetration of the graft by vessels is almost always preceded by haziness of the graft, the explanation of which might be the death of the keratoblasts, the antivascular substances being present only in living cells. The consequences of this explanation, if it should prove correct, may be very important. In any case, the security afforded by the latest techniques for partial and total keratoplasty provides an opportunity for the use of the action of the graft to clean up a cornea and to prevent the penetration of the vessels in evolutive keratitis.

Present-day indications for lamellar keratoplasties are (1) superficial keratitis, such as serpiginous ulcer, in which medical treatment has failed; (2) certain very severe ulcers, such as Mooren ulcer; (3) certain degenerative lesions—excellent results, for example, have been obtained by total lamellar keratoplasty in very large keratoconus; (4) all cases of interstitial viral keratitis, in which normal medical treatment has failed, provided the operation is performed before excessive vascular invasion has taken place; and (5) chemical burns of the cornea (alkali and others, especially bases). In these last, the process of removing the conjunctiva must be completed by removal of the superficial layers of the cornea; in addition to lamellar corneal grafts, grafts of buccal mucous membrane must be used to replace the tarsal conjunctiva in the burned eye, the bulbus itself being protected from any adhesion by a contact glass.

Many special precautions must be added to the normal technique in cases in which therapeutic lamellar keratoplasty is used. First, in order to prevent any damage to the graft and to the receiving cornea, the trephine must be sharp, the section made at a single stroke, and the use of forceps in placing the graft or the stitches avoided. Moreover, numerous edge-to-edge sutures are dangerous, not only because of the damage produced in the graft border and in the receiving cornea, but also because of the irritation caused by the suture material. Notwithstanding the massive use of cortisone drops or ointment, invasion of the graft by vessels or their penetration under the graft remains an important danger. Early roentgen or beta-irradiation cannot be used, because the rays are dangerous to the keratoblasts of the graft as well as to the vascular nodules, and living keratoblasts are perhaps the best protection against vessel penetration. Conjunctival overlapping, as suggested by Paufique, is apparently more suitable, at least in case of a superficial vascularization.

Many additional improvements will undoubtedly follow those already secured in corneal surgery by the new techniques of lamellar grafting so largely due to the work of Paufique.

THE INTRAOCULAR PRESSURE

CORRELATIONS OF THE SYSTEMIC AND INTRAOCULAR EFFECTS OF DIAMOX

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Many opinions have been expressed in favor of the theory that Diamox causes a fall in intraocular pressure by virtue of its local inhibition of carbonic anhydrase within the eye. There has been very little attempt to correlate the ocular effects of Diamox with its extensive systemic action, i.e., in causing diuresis and an increased excretion of electrolytes, especially of sodium and potassium.

Since water imbibition causes a rise in tension, it might well be expected that diuresis would have the reverse effect and that the loss of sodium, an ion which is intimately associated with the retention of water within the body, might also be expected to favor the loss of extracellular fluid not only from the blood but from the eye.

A single dose of Diamox (250 mg. or more) will produce its systemic effects almost immediately; these last for 24 hours, but on subsequent days or with repeated doses occur to only a slight extent. The patient is left in a state of acidosis which persists after diuresis has ceased. In the treatment of cardiac edema or of glaucoma, the patient may become resistant to the action of Diamox. Some cases of glaucoma are resistant from the outset. These phenomena are still unexplained.

In the present series of experiments the effects of a single dose of 250 mg. Diamox by taking simultaneous records of intraocular pressure of the amount and rate of diuresis and of the variation of sodium and potassium in the blood and urine were studied.

The results show that, whereas there is a variation in the degree of fall of intraocular pressure as between one subject and another after a single dose of Diamox, the response in each eye of any particular subject is remarkably alike, even when one eye had been trephined.

Although the maximum fall in intraocular pressure observed in active glaucoma is greater than in quiescent glaucoma or in normal subjects, the percentage fall is of the same order in all three groups. Furthermore it coincides with the period of maximum increase in the urinary output of water and of electrolytes (Na^+ and K^+), and with a fall in the level of serum sodium.

These facts suggest that the fluctuations of intraocular pressure which occur may be an intrinsic part of the osmotic changes which affect the body as a whole and that any speculation as to the mode of action of Diamox upon the eye should therefore allow for the systemic effects of the drug.

The findings concerning the effect of Diamox on urinary excretion confirm those of Lepri and Andreani (Arch. ottal., 1955, *58:* 313), who observed a similar diuresis in both normal and glaucomatous patients, but are contrary to those of Leydhecker and Helferich (Klin. Monatsbl. Augenh., 1955, *126:* 323), who found that after a dose of Diamox the minimum intraocular pressure was reached *before* the onset of diuresis, the volume excreted after 750 mg. Diamox being only 100 to 150 ml. in the first three hours.

In several of our glaucoma subjects the fall in intraocular pressure was actually commensurate with the volume of urinary output.

In two cases of quiescent glaucoma a very small output of urine and of electrolytes was accompanied by a correspondingly small decrease in intraocular pressure, while this phenomenon was also seen in the hysterical subject in whom antidiuretic factors arising from emotion may well have overcome the systemic effects of Diamox.

One might conclude from these observations that the loss of an appreciable volume of body fluid alone would account for a coincident fall in intraocular pressure, particularly in view of the fact that the imbibition of a similar amount of water (now in use as a provocative test for glaucoma) will so readily promote a rise in intraocular pressure.

But Becker (1955) has shown that Diamox will still bring about a fall in intraocular pressure within two hours in nephrectomized rabbits. Although the responses of such animals may not bear a close resemblance to those of human beings with normal renal function, his experiments suggest that the fall in intraocular pressure is not the direct outcome of increased urinary output, but it may nevertheless be associated with changes in the distribution of fluid and of electrolytes within the body.

In the human subject on a controlled intake of water and sodium, it is possible to gain some idea whether such changes occur by comparing the progressive alteration in composition of the blood and of the urine.

The blood may be considered to be an integral part of the extracellular fluid of the body. If the initial volume is taken as 15 liters, its initial sodium content will be 15 $\times$ the initial level of serum sodium. In any ensuing period (e.g., in 1 hr., 2 hr., and 7 hr.) it is possible to estimate the resultant concentration of sodium in the extracellular fluid by a calculation based on the actual intake and output of water and sodium during the period.

Two examples show that, whereas the estimated level of extracellular sodium remains remarkably constant, the level of serum sodium, as found by analysis by the flame photometer, shows a fall. This was the case in each individual subject, whether normal or glaucomatous. The degree of fall is outside the experimental error and is larger, in both normal and glaucomatous subjects, than any diurnal variation. It suggests that an alteration occurs in the extracellular fluid which is due either to the loss of sodium, or more probably to the gain of water from the intracellular fluid.

Comment: These findings suggest that since the decrease in intraocular pressure in both normal and glaucomatous eyes coincides with the period of maximum urinary output

of water and sodium and potassium, and a fall in the level of serum sodium, the effect of the drug is osmotic and that the mode of action may be general rather than local.

The subjects were 5 normal and 9 glaucomatous patients. It is important to note that the latter were divided into active and quiescent groups, the active consisting of 2 congestive cases and only 3 simple glaucoma patients. The quiescent glaucomas were 4 in number, all simplex. The criterion of quiescence was a pressure above 26 mm. on admission but which fell to this level or below after two days' rest in bed. The authors point out that glaucomatous patients excreted a slightly smaller volume of urine and sodium and potassium than did normal subjects.

The work of Maren and Wadsworth (Fed. Proc., 1954, *13:* 383) showed that the diuretic effect of Diamox may be prevented by the pre-administration of ammonium chloride to dogs but the fall in intraocular pressure is not thus affected. This same effect occurs in man. Becker's (Am. J. Ophth., 1955, *39* (*II*): 177) work on nephrectomized animals, with tonography in humans and rabbits, and chemical studies, especially the reduction in bicarbonate excess in the posterior chamber, indicate that Diamox causes a suppression of aqueous formation of about 60 per cent. The repeated oral administration of Diamox every 4 to 6 hours results in a cessation of the diuretic effect after the first 24 to 36 hours but the ocular hypotensive effect persists. This loss of diuretic effect is of advantage as far as the glaucoma patient is concerned because it avoids the problem of acidosis as a clinical consideration.

H. Saul Sugar

A COMPARISON OF SURGICAL AND CONSERVATIVE TREATMENT IN GLAUCOMA SIMPLEX

T. A. S. Boyd

Edinburgh, Scotland

Tr. Ophth. Soc. U. Kingdom, 1955, *75:* 541–560

The author undertook to compare conservative and surgical treatment in glaucoma simplex, using the deterioration in visual fields as a measure of the success of treatment. Records from the year 1930 to 1953 covering all cases of glaucoma simplex treated at the Oxford Eye Hospital were examined and those that satisfied the following criteria were included in the survey.

1. In order to make sure that only patients with glaucoma simplex were selected, those in whom the tension never exceeded 30 mm. Hg were eliminated because some of them might have had Schnabel's cavernous atrophy.

2. Patients were also excluded if their records showed even the slightest suggestion of congestive glaucoma; if they had secondary glaucoma; if they had suffered operative complications of any kind; if their central vision deteriorated to less than 6/24 on account of cataract, whether as the result of operation or of other causes; if the tension remained uncontrolled by the treatment; and if their

records failed to contain all the relevant information for at least one year from the beginning of treatment.

The records available were the usual series of Bjerrum screen and perimeter charts. The screen records, though satisfactory for the clinical follow-up of individual cases, were not sufficiently consistent for use in comparing one case with another. In contrast, there was a surprising consistency in the perimeter records, which consisted of 3/330 white records of the peripheral fields made on the same Hamblin self-recording electrically illuminated perimeter, and they were therefore the only ones used. Although the limited measure of deterioration provided by the 3/330 fields was far from ideal, it did provide a count of the eyes whose fields had clearly deteriorated after surgical or conservative treatment as the case might be.

In each case the perimeter record made at the beginning of treatment was examined and the presence or absence of peripheral field loss was noted. This formed the base line from which later deterioration could be gauged. The charts made at the end of 1, 2, 3, 4, and 6 years after the beginning of treatment were then examined and any increased field loss was noted, i.e., loss additional to that noted at the outset. In answer to the suggestion that a fair comparison of the results of surgical and conservative treatment is impossible because the surgical cases must have been the severer or they would not have been subjected to operation, it may be said that there were three factors in the Oxford Eye Hospital which made it possible to compare the cases treated surgically with those treated conservatively without disadvantage to either. First, in the early years of the glaucoma clinic, wartime difficulties made it necessary to treat many patients surgically who could otherwise have been treated conservatively, Many patients with similarly severe glaucoma have been treated in recent years with miotics alone, and their peripheral field loss can thus be legitimately compared with that found in the earlier cases. Secondly, there has been a trend toward conservative treatment and this provides many cases treated conservatively that can be compared with similar cases treated in earlier years by operation. Finally, the Oxford Eye Hospital has three surgeons, each adhering to slightly different criteria for the treatment of glaucoma simplex. One favors operation, another favors conservative treatment, and the attitude of the third lies midway.

The surgically and conservatively treated eyes were sorted into groups according to tension and field loss at the beginning of treatment. These groups of eyes, substantially similar at first, were then compared for deterioration of field over six successive years. Analysis of all the relevant data seems to show that uncomplicated surgical treatment of glaucoma simplex carries a greater risk than conservative treatment, regardless of the severity of the condition. There are, of course, risks other than field deterioration to be considered, notably, surgical complications and postoperative cataracts. If the findings in this study are confirmed, it will be necessary to abandon the present indications for operation in glaucoma simplex and to frame new ones. Special care will have to be taken to differentiate this condition from congestive glaucoma, in which early operation is generally indicated.

Comment: Boyd's conclusions that surgically treated eyes lost more visual field than similar eyes treated conservatively over a period of six years is not in accord with the conclusions of previous authors, such as, Reese, Burke and Kronfeld and McGarry, nor with the conclusions of most clinicians. However, there is much food for thought here. In spite of the selection of cases so that there would be a fair comparison of surgical and conservative treatment, one cannot help but feel that the choice of eyes to be operated upon must have had some relation to the severity of the disease or to greater difficulty in control of the ocular tension.

The one plaguing factor which probably is most important in evaluating surgical versus conservative treatment of simple glaucoma is the high incidence of surgical complications, both early and late. Boyd did not include cases of early complication; however, the increased tendency to cataract formation which appears to be present in some cases would tend to add weight to the author's conclusions, especially since lens changes of even relatively minor degree often interfere materially with the visual fields, particularly the perimetric ones which were used by the author.

A more recent paper on the surgical prognosis in glaucoma simplex by G. Bennett (Acta ophth., 1956, *34:* 73) adds further pessimism to the surgical outlook in these cases. Bennett concluded that over 60 per cent of cases showed further visual failure over a 1 to 16 year period. The remoter the operation became in time, the greater was the incidence of visual deterioration. In general, he stated, the outcome does not depend on the stage at which the operation is done, nor on the type of operation.

That there is some fear of the poor surgical prognosis has led this reviewer to express himself that in the treatment of simple glaucoma he would prefer at times that only one eye be operated upon. Only if this is considered successful after a period of one to three months, should surgical treatment of the other eye be considered. The idea of operating upon one eye only and treating the other medically has suggested itself many times.

In the discussion Boyd expresses the belief of J. P. F. Lloyd that some cases of glaucoma simplex may run a self-limiting course. This is not the general experience of clinicians and may be the result of observing marked increase in ocular tension during periods of psychic stress which later is relieved and leads to reduced, more easily-controlled tension.

H. Saul Sugar

THE STALLARD IRIDENCLEISIS OPERATION

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Arch. Ophth., 1956, *55:* 676–680

Stallard's operation, which he called anterior flap sclerotomy with basal iridencleisis and which the authors prefer to call a Stallard iridencleisis, was performed on one or both eyes in 48 patients (62 eyes) in the 40- to 80-year age group. Only patients with chronic primary glaucoma for whom surgical treatment was indicated and who would otherwise have been considered likely candidates for the

Elliot trephination, iridencleisis, Lagrange's or Iliff's sclerectomy, or other types of filtering operations were selected for this procedure. Moreover, most of the patients were white, because the authors prefer to use an Elliot trephination in Negroes. It is their impression that a larger, round opening is less likely to become obstructed in the Negro than is a wound with inclusion of a part of the iris, possibly because Negroes throw out more pigment and are more apt to have a keloid type of scar formation than are members of the lighter colored races.

The operation can be performed quite satisfactorily with local anesthesia, using an O'Brien block with tetracaine or Ophthaine by instillation. A retrobulbar block is not used, since it is not necessary to control pain and such a procedure would have the disadvantage of lowering the intraocular pressure. Experience has shown that a high-normal or slightly elevated tension makes iris inclusion surgery less difficult than if the eye has normal tension or is hypotonic at the time of surgery; consequently, a miotic is not usually given on the day of operation, although a miotic pupil is desirable at the time of surgery.

After routine preoperative preparation of the lids, the eye is draped, a speculum is inserted, and an antiseptic flush is used. A suture is then placed under the superior rectus muscle. A small amount of procaine is then injected beneath this muscle. Care is taken not to penetrate the superior rectus with either the suture or the injecting needle, as a hemorrhage in this muscle can be an annoying complication of the surgical procedure. An incision 8 to 10 mm. long, located at the insertion of the superior rectus tendon, is made through the conjunctiva and Tenon's capsule down to bare sclera. A flap is then dissected down to the limbus, and all bleeding is controlled with pressure and/or epinephrine. A cautery is used only if absolutely necessary. A scratch incision is then made 3 mm. from the limbus and parallel with it. When this scratch is approximately one-half to two-thirds of the way through the sclera, a traction suture—000000 nonabsorbable (silk) surgical suture—is placed through the anterior scleral lip of the incision. Hemorrhage, if any, is controlled again at this point, because most of the blood in a chamber after operations of this kind seeps in from the outside, and it is easier to keep it from entering the chamber than it is to remove it after it has gained entrance. The scratch incision is then continued until the base of the iris is seen. The direction of the incision should be at right angles to the surface of the globe at the line of incision; consequently, since the eye is rotated downward, the handle end of the knife should be angled from the vertical toward the feet of the patient. A narrow cyclodialysis spatula is used to check the extent of the incision depth. Ideally, when the grayish-black root of the iris or the beginning of the ciliary body comes into view, the spatula is used to dialyze the ciliary body from the scleral spur. Care must be taken not to penetrate the base of the iris or the embarrassment of having the spatula behind the iris will result. This complication is not always easy to avoid in cases of long-standing narrow-angle glaucoma with a dense synechia. The best way to avoid it is usually to hug the inner scleral and corneal surfaces closely as the spatula enters the eye. The cyclodialysis is performed by repeated poking thrusts to lessen the danger of hemorrhage. As soon as the cyclodialysis has been completed as far as can be

reached in either direction from the incision (usually one-third or less of the circumference of the globe), the scleral incision is hinged. The hinge is made in such a way that the width of its base is narrower than the original incision. This convergence is important in maintaining mobility of the flap on its hinge, because the flap fails to move on the hinge if it is made with parallel cuts. Indications are that the secret of success is the scleral hinge, which, when held open by the iris, produces a better fistulous tract. The chamber is then irrigated to remove any blood it may contain, and a toothless iris forceps is used to grasp the iris and withdraw it until the sphincter is seen at the surface of the incision. Straight iris scissors are used to cut the iris between the forceps and the sphincter of the pupil. This incision is from 2 to 3 mm. in length. A second incision in the iris is then made directly toward the base of the iris at one end of the original iris incision and a third incision is made at the other end. In effect, this produces a dialyzed ciliary body without dialysis of the base of the iris from the ciliary body, the iris sphincter remaining intact. The peripheral half of the iris for a width of 2 or 3 mm. has a flap which is hinged at its base. The iris flap is then left incarcerated in the wound with the pigmented undersurface of the iris now facing upward. Gentle irrigation or light corneal massage with an iris spatula is used until the pupil becomes round, indicating no lines of tension on the included piece of iris. The original incision is closed with a running black 000000 nonabsorbable (silk) surgical suture, care being taken to include Tenon's capsule as well as the conjunctiva in the closure. No drops are placed in the eye at the completion of the operation. Only the eye operated on is patched. A wet cotton splint is used and a shield is applied. The chamber is usually formed at the first dressing 24 hours later, at which time the pupil is dilated with 4 per cent homatropine hydrobromide. Hydrocortisone drops are used daily at rounds. The patient is up and around two days after the operation and is discharged on the third or fourth day, usually on hydrocortisone drops only. No massage is used.

Although the total number of eyes operated on is small and the average follow-up period of 22.4 months is relatively short, the results obtained in this series are encouraging: glaucoma was controlled in 58 (93.5 per cent) of the eyes, and only 27 of these required miotics after the operation to maintain normal tension without loss of vision or reduction of the visual field. In three of the four failures, the glaucoma was secondary and the operation was therefore not fully indicated.

Comment: Two comments may be made regarding the operative procedure advocated by the authors. The first concerns the value of a method whereby pressure on the incarcerated iris is relieved, and the second concerns the cyclodialysis portion of the procedure.

The usual iridencleisis procedures are generally held to be successful when a pigment-epithelial lined tract develops which permits aqueous to escape into the subconjunctival tissues. In order to prevent the pressure of the scleral lips from obstructing this escape many ophthalmologists have used techniques such as crowding the iris against one or both edges of the scleral clef or incorporating a posterior or anterior sclerotomy. Stallard's flap sclerotomy serves the same purpose. As such it is a reasonable and probably a very good procedure. The results of the authors certainly indicate its efficiency.

As regards the cyclodialysis portion of the procedure, it is my impression that the

cyclodialysis is not expected to function as a drainage pathway but rather makes possible the scleral flap which begins 3 mm. from the incision and is, therefore, behind the ciliary body insertion. The iris, which is pulled up into the scleral cleft, would tend to close off any supraciliary pathway. For this reason it is understandable why Stallard did not include the term *cyclodialysis* in his name of the operative procedure: "Anterior flap sclerotomy with basal iridencleisis."

H. Saul Sugar

SOME RESULTS OF THE PREZIOSI OPERATION

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Brit. J. Ophth., 1956, *40:* 222–224

A simple glaucoma operation which can be consistently successful is still needed. The nearest approach to this from the point of view of ocular tension would appear to be the anterior flap sclerotomy with basal iridencleisis, (see the preceding article by Mulberger and McDonald) but this is a technically difficult operation requiring very great skill. After various trials with measures on the ciliary body, attention is returning to simple drainage as in the trephine but using other methods of making the filtration hole, e.g., diathermy.

The Preziosi cautery method (Brit. J. Ophth., 1924, *8:* 414 and Acta XVI Concilium Ophth., 1950) appears to have been introduced originally as a safe method from the point of view of sepsis, but its general use was discontinued so long ago that it is rarely mentioned in the current textbooks. The series reported here began in 1951, and the results have been so impressive that the operation has replaced nearly all previously used procedures in the writer's practice. The method is not fraught with the obvious danger of thermal cataract that immediately springs to mind, and appears to give rise to no serious complications. The anterior chamber takes some time to reform, but no massage is required, a good bleb forms, and the ocular tension remains at 25 mm. Hg or less in over 90 per cent of cases of chronic simple glaucoma.

OPERATION

After the introduction of a speculum, a superior rectus suture is inserted. Reflexion of the conjunctiva follows as for a trephine and may be done with the cautery. With the cautery, contraction of the conjunctiva might be expected, but the dissection is clean, and the whole cautery sequence is unexpectedly interesting from a surgical standpoint. The ordinary galvano-cautery point at red heat is passed through the limbus into the angle by one or more sweeps, as in an *ab externo* approach, until the aqueous escapes. There is no possibility of damage to the underlying structures as the aqueous cools the cautery. The

puncture should be large enough to admit an iris repositor into the anterior chamber, but if not it may be enlarged with cautery of de Wecker's scissors. The iris may or may not be burnt. Should it prolapse into the puncture hole it is perforated with the cautery and then replaced. Another method which was used at first was to use the cautery as a keratome, but this method was later abandoned because it showed no improvement on the *ab externo* approach. The cautery is bent to a keratome angle and may then be passed like a keratome, but more rapidly into the angle. It may reach as far as the pupil, cooling being instantaneous. If the iris does not present it may be withdrawn and an iridectomy performed or a pillar may be brought out for inclusion. The conjunctival wound is closed, atropine and an antibiotic is instilled, and a single dressing given.

RESULTS

Between 1951 and 1954, 46 eyes were operated on, 31 for chronic simple glaucoma and 11 for secondary glaucoma. The intraocular pressure, unless obviously low, has been taken by tonometry, 25 mm. Hg or below being taken as normal. In the chronic simple cases, after a period ranging from 3 months to 3 years (average 2 years) since the operation, 93 per cent (29) have normal tension, and 5 have normal tension although ceasing to drain.

In the cases of secondary glaucoma, the results were varied. There were two hemorrhagic cases which were both failures. Of two aphakic cases one is satisfactory and one has not been traced. Of six cases of uveitis, only one failed.

Complications

(1) *Choroidal Detachment.* This was seen in 25 per cent of the "keratome type" but not in the *ab externo* type. It invariably settled down but might take a long time; in one case each eye took nine months. It may be so large that the two sides of the retina nearly meet, but it is no contraindication to discharge. Comparison of the pre-operative and eventual postoperative fields showed no change.

(2) *Hyphema.* This never amounted to more than a few patches on the iris, and only followed a scissors iridectomy.

(3) *Iris Impaction.* This may occur if there is no iridectomy and may be seen but may cause no symptoms on the following day. The flap should be raised and the prolapse either perforated by cautery and replaced or an iridectomy performed. This happened only twice in the first few "keratome type" cases.

(4) *Injury to Lens.* This occurred in one case only, through misdirection in a case of the "keratome" type. A dense white scar, the pattern of the cautery point, resulted; it gradually faded over 2½ years and is now difficult to see.

(5) *Bleb Infection.* This happened twice in one eye and was easily controlled.

(6) *Iridocyclitis.* A pigment disturbance is occasionally seen. Posterior synechiae may arise if atropine is omitted, but they may be ruptured by mydricaine. One severe case of cyclitis and rapid maturation of cataract arose some months after operation.

Comment: It is remarkable that an operative procedure which gives results as good as those reported for it not only by its author but by the author of this paper, Neame (Acta XVI Concilium Ophth., 1950, 975) and Frankhauser and Schmidt (Ophthalmo-

logica, 1956, *131:* 342) should not have been used in the United States. At least, no reports of its use have appeared. It is, however, understandable in view of the fear of damage to the lens and stimulus to scar tissue formation.

Neame carried out the Preziosi procedure in 20 cases, 17 of whom were followed up. Persistent normal drainage resulted in 13 cases. Of the 4 failures, one had been previously operated upon, 2 had glaucoma following cataract extraction and 1 was a diabetic.

Neame compared the effect of electro-cautery at dull-red heat with a diathermy puncture with a pointed needle for 6 seconds each on a cadaver liver. He found the actual necrosis greater with cautery than with the diathermy, but the area of surrounding damage is greater with the latter.

Preziosi dissects the conjunctival flap with a cautery, although Kelly, too, states that it may be done in this manner. A wire cautery point 0.5 x 1.0 mm. in size is used and directed toward the chamber angle with an *ab externo* approach. Iridectomy with the cautery is performed by Preziosi only when the iris bulges into the aperture or tends to prolapse.

According to Preziosi the results were most satisfactory when the operation was performed to lower intraocular tension. In the case of blind painful eyes, the operation succeeded in relieving congestion and pain but the tension did not usually reach normal limits. The results were disappointing only in hemorrhagic glaucoma and glaucoma complicating diabetic retinopathy. The puncture had to be repeated on rare occasions. In only a few were miotics necessary postoperatively.

Kelly's results are in accord with those of Preziosi who performed the operation in 665 eyes for different forms of glaucoma: 274 simple, 88 acute, 55 chronic congestive, 19 hemorrhagic, 15 traumatic, 44 secondary to cataract extraction, 65 other secondary glaucomas, 8 buphthalmos.

Frankhauser and Schmidt reported that of the glaucoma simplex cases operated at the Berne Clinic in 1953, 70.5 per cent of 25 cases in 1954, and 93.8 per cent of 16 cases in 1955. No lens opacities were found.

In view of the excellent results reported, it might be wise to compare this method with the usual method of surgical treatment in teaching institutions, with facilities for adequate evaluation.

H. Saul Sugar

SECTORAL DISTRIBUTION OF GONIOSYNECHIAE

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Brit. J. Ophth., 1956, *40:* 129–135

Gonioscopic observations for patients with glaucoma selected from the first 1,600 attending the Glaucoma Clinic at the Institute of Ophthalmology were studied for the purpose of ascertaining whether the goniosynechiae in glaucomatous eyes are distributed at random or whether, as clinical impression suggests,

they tend to occur more in the upper than in the lower half. Patients were chosen for this study only if they fell definitely into one of the following diagnostic categories: (1) acute closed-angle glaucoma; its preglaucomatous stage; the quiet phase following an acute attack if resolution had occurred without surgical intervention; (2) chronic closed-angle glaucoma; and (3) simple glaucoma. No eye with goniosynechiae was included if there was a history of previous operation, perforating injury, or inflammation. If any doubt existed about the presence of synechiae, or if (as in a few cases) no specific note was made of their actual position, the eyes in question were excluded.

Very few eyes with closed-angle glaucoma were examined in the acute hypertensive state. Most of the eyes included in the first category had, therefore, previously suffered an episode of hypertension which had resolved without operation, or had experienced the recurrent premonitory symptoms of a rise of tension, and/or had shown positive results with provocative tests.

When records of a suitable case were found, the presence of a synechia in a given sector of the angle was indicated by a dot in the appropriate part of a concentric histogram. For example, if synechiae between 10 and 2 o'clock were recorded on a gonioscopy case-sheet, a dot was placed in the sector corresponding to each of the 10, 11, 12, 1, and 2 o'clock positions; the radial lines from the center of the clock face cut the circumference at each half-hour. The next suitable eye in the same diagnostic category was treated in the same way and credits were made in the same diagram, the composite histograms for right and left eyes being kept separate. For the purposes of this study it was not necessary to differentiate between a small synechia and extensive synechiae within a given sector, a single credit being placed on the diagram in each case.

The composite histograms thus obtained show that goniosynechiae are not distributed at random round the angle in cases of acute and "subacute" closed-angle glaucoma, but that they tend to occur mainly above, the highest incidence being probably a little to the temporal side. This peculiarity has not been statistically proved to occur in cases of chronic closed-angle glaucoma or of simple glaucoma, but the same tendency probably exists in these eyes.

CLOSED-ANGLE GLAUCOMA SIGNIFICANCE OF SECTORAL VARIATIONS IN ANGLE DEPTH

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Brit. J. Ophth., 1956, *40:* 136–143

Although unstable vascular or nervous systems may exist in patients with closed-angle (congestive) glaucoma and may play a part of undetermined importance in the disease, the vast majority of eyes so affected admittedly show an

inherited shallow anterior chamber and a forward ballooning of the iris produced by resistance to the flow of aqueous between lens and iris. This resistance is due to the close contact between these two structures imposed on them by the forward position of the anterior surface of the lens. As time passes and the lens increases in size, the ballooned iris is pushed forward and its periphery gradually approaches the trabeculae; an "attack" of glaucoma may occur as a result of pupillary dilatation, a change in position of the iris root, a change in the curvature or position of the lens, or any factor which alters the pressure on the two surfaces of the iris so that it is pushed, or pulled, on to the trabeculae over a wide enough area to embarrass drainage of the aqueous humor. It is also generally agreed that a peripheral iridectomy, or even an iridotomy, will relieve the symptoms by allowing the aqueous to by-pass the pupil so that the angle will open as the iris bombé disappears: the classical broad iridectomy achieves the same result but adds an unnecessary trauma to the sphincter pupillae.

Evidence has been adduced to show that goniosynechiae in closed-angle glaucoma occur especially in the superior half of the angle of the anterior chamber, a finding which confirms the clinical impression that the angle is almost invariably shallower above than below. Barkan has observed that both the normal and the narrow angle show this phenomenon and he suggests that it may be due to the weight of the column of aqueous in the anterior chamber. The same anatomical peculiarity was also remarked by François.

Gonioscopic and other findings illustrating the fact that the angle of the anterior chamber is shallower above than elsewhere and clarifying the part played by this phenomenon in the natural history of closed-angle glaucoma were obtained in two patients with closed-angle glaucoma and one who had the premonitory symptoms of the disease. As a result of his findings, the author suggests that, in eyes which are in danger of ultimately being affected by closed-angle glaucoma, iridocorneal contact begins above long before there are any symptoms, and progresses slowly downwards as the lens increases in size with age. When the free angle becomes reduced nearly to the critical amount for adequate aqueous outflow, the premonitory symptoms are produced by transient increases in the area of trabeculae covered by iris. Provided that there has been no inflammatory reaction in iris or cornea, this contact superiorly may remain for years without being converted into permanent synechiae. These new conceptions make it easier to understand total closure, and hence acute closed-angle glaucoma, resulting from sudden occlusion of the small amount of residual angle left open below. Measurements of the depth in various parts of the shallow anterior chamber before and after peripheral iridectomy have shown that, while the lens remains stationary, the iris sinks backwards away from the cornea. The main factor causing the anterior chamber to be shallower above may be greater peripheral flattening of the cornea in that region. This in turn may be due to pressure of the upper lid.

In one of the three patients reported on, resolution of the closed-angle glaucoma resulted from marked shortening of the superior segment of the iris which allowed the aqueous to escape through the pupil at 12 o'clock and thus eliminated the iris bombé. The eye, therefore, may be said to have successfully performed

upon itself the equivalent of a central iridectomy. The vertically oval pupil in acute closed-angle glaucoma may be an "attempt" by the congested eye to achieve resolution.

Comment: These two papers from the glaucoma clinic of the London Institute of Ophthalmology are typical of the systematic investigation and classification that is being carried out there in the study of this disease. This is the first statistical study showing that goniosynechiae are most frequent above although the fact that the upper portion of the angle is its most narrow part has been recognized clinically since it was first described by Barkan. Phillips' finding that goniosynechiae also tend to be more prevalent on the temporal side is interesting and new.

The suggestion that the pressure of the lid as a cause of flattening of the cornea and, consequently, of the narrowness of the angle above is reasonable and well presented.

The only objection which may be raised to this study is the large number of synechiae found in cases of simple glaucoma. Actually the study concerns 20 right and 27 left eyes in acute or pre-acute angle-closure glaucoma and 25 right and 24 left eyes in simple glaucoma. The incidence of synechiae in simple glaucoma is exceptional and most authorities believe that they are found only in very late stages of the disease.

H. SAUL SUGAR

DIAMOX TOXICITY

A case of marked bone marrow depression after treatment with Diamox is reported in a 73-year-old man. Death was due to agranulocytosis and thrombocytopenia with marked hemorrhagic diathesis. The author points out that an individual idiosyncratic reaction to any chemical can occur in a given patient and that this compound chemically related to the sulfonamides is capable of producing bone marrow changes, with fatal agranulocytosis and thrombocytopenia.

LEE C. UNDERWOOD

J. A. M. A., 1956, **161:** 1477–1478.

LACRIMAL SYSTEM

LACRIMAL DISEASE ASSOCIATED WITH INFECTIOUS MONONUCLEOSIS

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Tr. Ophth. Soc. U. Kingdom, 1955, *75:* 101–119

Glandular fever is a common, but extremely variable, infectious disease which may appear as a clearcut fever with lymphadenitis, or may assume any one of several forms according to the particular system, tissue, or organ affected. Its variable manifestations are usually, but not always, accompanied by some degree of fever. Glandular enlargement is usually present, but may be transient, or inaccessible to examination; splenomegaly is often found.

The disease is characterized by the development of a temporary mononucleosis, that is, an increase in the total of all types of mononuclear white cells to more than 50 per cent of the differential count in the absence of a leukopenia, and by the appearance of abnormal large lymphoid cells in the blood. These cells, which have been described and beautifully illustrated by Downey, vary in size, have a foamy vacuolated or granular basophil cytoplasm with a nucleus that is round, indented, or bizarrely lobed in shape. The chromatin pattern is of the mature dense lymphoid type except on occasions when more immature nucleolated forms appear. A few abnormal lymphoid cells may appear in the blood in a variety of virus diseases and in acquired toxoplasmosis.

A positive Paul Bunnell reaction of more than 1:64 is practically diagnostic but a negative one does not exclude the condition, since the reaction may be positive for only a short time or may only become positive during a recurrence. In addition, there may be one type with positive and one with negative Paul Bunnell reactions.

From the ocular point of view, 4 patients out of 13 presenting with dacryoadenitis were found by the author to have glandular fever. Although he has not investigated older patients for glandular fever, it seems probable that a fair proportion of cases of acute dacryoadenitis in young people at least may be explained by its presence. Conjunctivitis is commonly said to occur in 10 per cent of all cases of glandular fever, and since in a series of 102 patients with eye complaints 3 had dacryoadenitis and 2 dacryocystitis, it may be assumed that the incidence of each of these complications will be about 1 in every 300 cases.

The lymphatic and reticuloendothelial tissues of the body may be attacked in a patchy and successive way by this disease wherever they lie, be it in the lymph nodes, the spleen, the ocular, respiratory, or alimentary mucosae, or in parenchymatous organs such as the lacrimal or salivary glands and the liver.

The lacrimal apparatus may be affected in various ways by an infectious mononuclear inflammation of the ocular adnexa; thus some patients will have dry eyes and others will have watery eyes. Apparently, the conjunctivitis itself does not occasion epiphora; various additional factors, however, may provoke it. These factors are (1) reflex hypersecretion, (2) hypersecretion from inflammation of the gland, (3) malposition of the punctum, (4) impairment of drainage by dacryocystitis, and (5) impairment of drainage as a result of rhinitis.

Dacryoadenitis presenting essentially the same clinical picture, but varying in severity, was found in 4 patients with infectious mononucleosis 3 of whom were treated in the Ophthalmic Department of the Dunedin Hospital and 1 at Moorfields. In each there was an acute unilateral, very tender, palpable enlargement of both orbital and palpebral lobes of the lacrimal gland. The pain often came in severe jabs as well as in a dull ache. The tenderness extended over the orbital margin along the zygoma. In each there was lymphadenitis extending beyond the field of drainage of the lacrimal gland and in one the spleen was enlarged. The blood picture of infectious mononucleosis appeared. In 1 case the Paul Bunnell test was positive, in 1 it was negative, and in 2 it was not performed. Lack of response to treatment was noticeable, since the 2 severe cases worsened in spite of penicillin and sulfonamides, and the 2 mild cases improved without any treatment.

Three clinical pictures other than the one presented by these patients may also be expected in infectious mononucleosis: (1) acute bilateral dacryoadenitis; (2) acute dacryoadenitis with salivary adenitis; and (3) subacute or chronic dacryoadenitis. Biopsy material taken from the conjunctiva in infectious mononucleosis sometimes shows infiltration around the lacrimal excretory ducts; again, in other places, the ducts are actually invaded by the infiltration. The patchy way in which the lymph nodes become involved suggests that the disease is one that spreads by way of the blood rather than by continuity. The normal occurrence of lymphoid tissue in the lacrimal gland in islands between the acini and lobules, or around the ducts, makes this gland an obvious possible target for the disease. It is thus quite unnecessary to insist on spread from an inflamed conjunctiva up the lymphatic spaces around the ducts to the gland.

The ocular symptoms of patients with infectious mononucleosis often overshadow their rather vague systemic illness, so that the making of a correct diagnosis depends largely on an awareness of the disease, careful interrogation, repeated general physical examinations, and blood studies.

Comment: In discussions of the ocular complications of infectious mononucleosis, emphasis is usually placed on the occurrence of conjunctivitis. It is estimated that approximately 10 per cent of all cases of infectious mononucleosis develop conjunctivitis. Involvement of the lacrimal or salivary glands is a rare complication of this systemic disease.

From the point of view of etiology of inflammation of the lacrimal gland, however, it is of interest that the author reports 4 patients with infectious mononucleosis out of 13 patients presenting with dacryoadenitis. This is of considerable importance for it means that one must consider infectious mononucleosis in the differential diagnosis in every case of inflammation of the lacrimal glands. The diagnosis can be established with reasonable

certainty on the basis of lymphadenopathy, splenomegaly, abnormal lymphocytes in the peripheral blood, and a positive heterophile agglutination. Since this disease process has a good prognosis and there is no specific therapy, it is important for the ophthalmologist to be aware of this cause of dacryoadenitis.

BERNARD BECKER

THE CLINICAL FEATURES AND ETIOLOGY OF DACRYOADENITIS

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Tr. Ophth. Soc. U. Kingdom, 1955, *75:* 435–452

On the basis of data obtained in 16 cases of lacrimal gland inflammation, an attempt has been made to assess the frequency of glandular fever as a cause of dacryoadenitis, to sort out the causes in cases not due to glandular fever, and to correlate the clinical features with the cause. The various diseases responsible for dacryoadenitis may be classified according to their route of infection as follows: (1) invasion by way of the ducts; (2) invasion by way of the nerves; and (3) invasion by way of the blood.

In considering invasion by way of the ducts, it should be remembered that the lacrimal gland is arranged in two lobes so that one, the orbital lobe, drains into the conjunctival sac through the long ducts and the other, the palpebral lobe, drains through the short ducts or else empties into the longer ducts of the orbital lobe. In either case, an ascending infection is more apt to cause inflammation of the palpebral lobe. The invading organisms may come from a frank conjunctivitis or simply from transitory organisms that have gained access to the conjunctival sac. By far the commonest are the staphylococci. The 6 patients with staphylococcal infections presented the following features: (1) There was a heavy growth of coagulase-positive staphylococci from the conjunctival sac in all, with the exception of 3 cases in which antibiotics had been used; (2) 2 cases were preceded by boils, and 1 by styes; (3) all were unilateral; (4) the inflammation began in the palpebral lobe in all cases and remained confined to it in all but 2; (5) inhibition of abduction of the affected eye from pain was seen in 2 cases, but no paralytic squint could be domonstrated in them; (6) clinically, the process looked pyogenic. Tenderness was exquisite and more localized than in cases caused by viruses; (7) tenderness over the zygoma from pressure on the temporozygomatic nerve (Wilson's sign) was not present; (8) the systemic reaction was mild, and 3 patients had no fever; (9) the preauricular node was always enlarged, but the lymphadenitis was strictly a regional drainage reaction. Both lymphadenitis and fever responded very rapidly to penicillin; (10) at the height of the disease, there was a slight neutrophil leukocytosis in four cases.

Leukocytosis was not investigated in the others. There was no eosinophilia and no abnormal lymphoid cells were seen; and, (11) the total duration of the disease—one to two weeks—was shorter than in cases due to virus infection. Once the appropriate antibiotics were used, resolution within a week was the rule.

Affection of the conjunctiva in herpes zoster is determined by the nerve supply and occasionally the area supplied by the lacrimal nerve is selectively involved. Since the virus attacks the conjunctival epithelium, as evidenced by the typical acidophil intranuclear inclusions, it is not surprising that it should also attack the lacrimal gland epithelium, which is derived from this area of conjunctiva.

In considering invasion by way of the blood stream, it should be remembered that the lacrimal gland is composed of two different tissues: first, the essential secretory epithelium, and second, the lymphoid and reticuloendothelial tissue, both of which are subject to attack by viral and bacterial diseases. Dacryoadenitis in the first 3 of the author's patients, seen in Dunedin, New Zealand, was associated with infectious mononucleosis with negative Paul Bunnell reaction. Infectious mononucleosis was also present in the fourth patient seen in London, but in this case the Paul Bunnell reaction was positive. No other definite cases of this association have been found, although it may have existed in 1 patient with cervical adenitis who failed to return for a diagnostic follow-up. Two possible cases may be found in the literature, 1 in 1954 and 1 in 1890.

The Paul Bunnell negative cases probably represent infection by a different virus or group of viruses, rather than a different host reaction to the same strain. The whole group of cases of acute dacryoadenitis with lymphadenitis, to which these and the cases in the next group belong, may eventually be separable into three types: (1) true glandular fever with positive Paul Bunnell reactions, probably of sporadic occurrence; (2) infectious mononucleosis with negative Paul Bunnell reactions, probably of epidemic occurrence, and probably comprising a group of similar conditions; and (3) acute dacryoadenitis with lymphadenitis and eosinophilia, apparently sporadic, but possibly related to Toulant's epidemic disease. Infection of the third type, exemplified in 3 of 12 patients seen at Moorfields, resembles the glandular fevers in having an associated lymphadenopathy but shows blood changes of a different character. All 3 of these patients presented certain features in common: (1) acute unilateral dacryoadenitis involving both orbital and palpebral lobes; (2) marked weakness of abduction of the eye, with temporary choroidoretinal detachment in 2 cases; (3) mild lymphadenitis exceeding that explicable on the basis of a regional drainage reaction; (4) mild evening pyrexia lasting longer than the dacryoadenitis; (5) absence of evidence of infectious mononucleosis, toxoplasmosis, mumps, or staphylococcal infection; (6) lack of any convincing response to penicillin; and (7) eosinophilia of variable degree developing as the dacryoadenitis waned and resolving as the clinical features cleared up. The choroidoretinal detachments were an interesting complication which has heretofore apparently only been noted in syphilitic dacryoadenitis.

Complement-fixation tests showed that mumps could be excluded as a possible cause in all but one of these cases. Influenza is often mentioned as a cause of

dacryoadenitis, but the clinically suspicious cases in this series all occurred before the necessary serological tests to establish its presence could be arranged for. Finally, syphilitic dacryoadenitis was found in one patient, a 55-year-old woman, with syphilitic aortitis. Treatment with penicillin produced great improvement in both her general and her ocular condition, but she is to be kept under long-term observation, especially in view of her aortic incompetence.

The present series of 16 patients is not large, but it illustrates the fact that dacryoadenitis, though rare, is always a condition in which it is worth while to assess the patient as a whole

Comment: This report is valuable as it is unusual to be able to report experience with such a large series as 16 cases in any condition so rare as acute dacryoadenitis. It would seem advisable to add "acute" to the term as used by the author to disinguish this group from the chronic granulomatous tumor-like lesion of Mikulicz syndrome.

The classification according to the route of invasion is entirely logical and should be accepted. The clinical features of the various etiologic types are well described. It is not surprising that 6 of the cases are staphylococcal in origin, but that so many were complications of infectious mononucleosis seems unusual. That this disease was epidemic at this time might account not only for this but also for the relatively large series.

The author's statement that in this condition it is always worth while assessing the patient as a whole surely holds good for the chronic types as well as the acute disease.

T. E. SANDERS

THE LENS

OCULAR WOUND HEALING WITH PARTICULAR REFERENCE TO THE CATARACT INCISION

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Although the incidence of failure in cataract extraction has been greatly reduced by various technical advances, minor imperfections in wound healing still play a significant part in the production of serious sequelae. Recent experimental studies and clinical observations on the mechanisms of normal repair of a cataract incision not only have confirmed many of the findings of earlier histologists but also have supplied additional information about the healing of corneal wounds.

The primary closure of any corneal incision is effected by swelling of the corneal lamellae produced in large part by imbibition of aqueous humor. After this central contact has been established, the stromal surfaces soon become agglutinated and within three or four days keratoblastic proliferation is observed and stromal healing begins. In the initial stages the normal retractivity of the tissues produces separation of the anterior and posterior edges of the wound. In the presence of a conjunctival flap the anterior gaping surface is soon filled with episcleral fibrovascular tissue, the amount and depth of which is determined by the degree of separation of the wound edges. As stromal healing progresses, the plug of fibrous tissue becomes smaller by being pushed toward the anterior chamber.

The gaping posterior portion of the wound does not participate in the immediate repair. By the end of a week, when stromal proliferation has become well established, endothelial proliferation begins to bridge the defect produced by retraction and inward curling of the cut edges of Descemet's membrane. The slowness with which ocular incisions become completely healed was shown by Purtscher's microscopic studies of two eyes removed 14 and 15 days after cataract extraction. In both specimens the conjunctival flap was firmly closed by young scar tissue, but the corneal healing was still incomplete and limited to the anterior part of the wound. Maggiore in an extensive study of corneal wounds recorded similar findings after 10 to 12 days, and concluded that it takes two or three months for a cataract incision to heal completely. Studies made by Gliedman and Karlson in cats also corroborate the author's histological observations showing that the healing of limbal incisions is not complete for at least two months.

In considering the influence of sutures on wound healing, it should be re-

membered that it is essential for the surfaces of any wound to lie in apposition without distortion and without intervention of surrounding tissues if normal healing is to be obtained. In most incisions sutures are used, not to force together gaping surfaces, but to reinforce tissues already in proper apposition. The technique of suturing, as well as the material used, may vary but certain basic principles must be followed. Foremost in importance is the recognition that the immediate strength of a sutured wound depends, not on the tensile strength of the suture employed, but rather on the holding power of the tissues themselves. Therefore it is futile to use a suture with a tensile strength greater than that of the tissues into which it is inserted. Since all sutures by inciting foreign body reaction devitalize the tissues, their presence lowers the tensile strength of the structures in their immediate vicinity. For this reason the number of sutures used should be no more than necessary to maintain apposition. Studies of the reactions produced by sutures have shown that one of large size and great tensile strength is often not so effective as a finer one of lesser strength.

Although silk has long been the most popular suture material, the use of surgical gut is increasing. Many of the former objections to this absorbable material have been overcome through improved manufacturing techniques. The same improvements that have made it more acceptable in general surgery have also increased its usefulness in ophthalmic surgery. When silk is used as a suture material in ocular tissues, the initial responses are most promising, but the rapid proliferation of epithelium along the suture track and late stromal necrosis are unfavorable reactions which are strikingly absent when surgical gut is used. The vascular response provoked by surgical gut, however, is much greater than that produced by silk.

The effect of some of the newer drugs and hormones on wound healing is being investigated, but the differing results reported by various workers seem to show that further study is needed before their use can be generally accepted.

Many abnormalities of wound healing result from subsequent rupture of the incision. The term rupture as usually employed denotes a sudden separation of the wound, but in fact three degrees of rupture may be recognized: (1) gaping of the wound with edema of the conjunctival flap; (2) rupture of the wound with forcible tearing of the newly-formed capillaries and resultant hyphema; and (3) rupture of the wound with prolapse of iris. Although the first and second degrees have been dismissed as unpleasant but not often serious, they may lead to major complications. It has been possible to demonstrate experimentally that edema of the conjunctival flap is produced by fluid passing from the anterior chamber through the interstices of the wound. Seepage of this kind, however, seems to be harmless unless there is drainage enough to alter the depth of the anterior chamber. The incidence of delayed reformation or subsequent loss of the anterior chamber in the author's series of 800 cataract extractions was 13 per cent, which corresponds closely to Kronfeld's finding of 11 per cent. The postoperative administration of Diamox neither cured nor prevented this complication, nor did it influence the incidence of hyphema. Bleeding into the anterior chamber was noted in 20.6 per cent of the 800 cataract extractions. When silk was used its incidence was 17.7 per cent, whereas with mildly chromicized surgical gut it was

23.5 per cent. Microscopic study of 171 eyes removed after cataract extraction showed that faulty wound healing was the primary cause of the pathological process responsible for removal of the eye. The various processes were tissue incarceration, 31 per cent; stromal proliferation, 32.8 per cent; and epithelial invasion, 36.2 per cent.

Corneoscleral sutures have greatly reduced the complications resulting from gross imperfections in wound healing, but they have not done away with tissue incarceration and epithelial invasion of the anterior chamber—conditions frequently produced by slight malposition of the wound. Epithelial ingrowth, which has increased greatly in frequency of late, may be produced by improper suturing; consequently, attention to such details as depth of the bite, tightness with which the suture is tied, and early removal of nonabsorbable material should help to reduce its incidence

Comment: This is a most interesting and instructive paper. Probably every ophthalmic surgeon today uses some type of suture to close his cataract incision. There are not many, however, who are aware of the dangers of using heavy suture material, of taking too deep a bite with the suture, or of tying the suture too tight. They may wonder why the chamber is shallow with no demonstrable leak, or why the chamber shallows on the seventh or eighth day when the necrosis about the suture opens a fistula into the anterior chamber.

The suture should be placed no deeper than the anterior wall of the cornea and sclera. If a limbus based flap is used, one must be careful that conjunctiva is not pulled into the suture tract. Likewise, when the suture is tied, whether one uses a limbus or fornixed based flap, one must be certain that no tag of conjunctiva or episcleral tissue is incarcerated in the wound as the suture is tied. The suture should be tied snugly but not too firmly.

Despite the experimental evidence of the difference in the tissue reaction between silk and surgical gut, ophthalmologists will probably use that material with which they are most familiar. Surgical gut certainly provides satisfactory closure and avoids the necessity of removing sutures. It has one disadvantage in that it is more difficult to handle.

The local and systemic use of the corticosteroids in moderate doses apparently has no pronounced effect on wound healing. There is experimental evidence that fibroblastic activity is depressed by the corticosteroids in large doses. In clinical practice, however, ACTH and cortisone have been given preoperatively and postoperatively without any definite evidence of their adversely affecting wound healing.

Localized edema of the flap, especially near one of the sutures or between the sutures, is not an infrequent finding on the fifth to tenth postoperative day. Providing the chamber is formed and there is no evidence of incarceration of iris, it is usually of no consequence and gradually subsides. Persistence of a cystoid scar implies incarceration of a small piece of iris. These eyes usually manifest hypotomy and excision of the cicatrix may be necessary.

Hyphema is an annoying, but not necessarily a serious, complication. The more scleral the section, the greater the incidence of hyphema. This reviewer agrees with the author that it is usually caused by external pressure such as blepharospasm.

There is no question that the use of sutures has reduced many of the hazards of cataract surgery. Like anything else, they may be abused. One must be meticulous in placing them, and one must be careful in tying them lest they produce gaping of the wound and defeat the purpose for which they were employed.

P. Robb McDonald

CATARACTS ASSOCIATED WITH LOCAL AND GENERAL NEURODERMATITIS

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Association of cataracts of a presenile character with a dermatosis may exist in several distinct forms. Two of these, scleroderma with cataracts (Werner's syndrome) and poikiloderma with cataracts (Rothmund's syndrome), lie outside the scope of this article, as does also a relatively minor group in which cataracts have been noted in connection with such dermatoses as Darier's disease, erythema exudativa, Raynaud's disease, psoriasis, and others. The commonest group, which is the one now under consideration, comprises the cases in which cataract is associated with local and general neurodermatitis. These cases appear to have no hereditary or familial basis, always excepting a possible familial psychic instability and occasionally a familial allergic history, and are characterized by the skin lesions, which have been classified under many names, such as atrophy, allergic eczema, anaphylactoid dermatitis, prurigo diathesique, lichen simplex chronicus, and neurodermatitis, to name but a few. The last of these, qualified by the local or general prefix, seems to be the most apposite to the lesion. Characteristically, this appears in the first decade of life, usually as an eczematoid eruption of a weeping, oozing, and crusting nature, remissive and relapsing. As the patient grows, the lesions tend to become drier and more lichenified in type, resulting in a pale, thickened, hard, flaky skin, which in its quiescent phases has a quite characteristic feel to the fingertip, comparable to the feel of a slightly dry but tense grapefruit. Relapses into a wet eczema are not uncommon, especially under environmental stress. Pruritus with sometimes uncontrollable scratching is almost the rule, especially in relapses, and is responsible for the scarred appearance of the rash. Even in the more generalized form of the disease, the face and flexures, especially the cubital and popliteal, are the elective sites of the most persistent and pronounced rash.

The ocular lesions consist chiefly of thickening of the skin of the eyelids and of cataracts that appear suddenly, sometimes proceeding to maturity in a few weeks. Two main types are seen: (1) posterior and anterior subcapsular opacities that coalesce and spread to form a homogeneous cortical cataract, and (2) an anterior subcapsular opacity, often shield-shaped, with thickening and wrinkling of the anterior capsule which later spreads to the rest of the lens. This latter type appears to develop more slowly, taking a year or more to achieve full maturity. Cataracts of either of these types are said to occur in about 10 per cent of all cases of neurodermatitis. They are commonly bilateral, with a short time-interval between the onset in each eye, but a figure of 30 per cent has been given for unilateral cases. They may occur at any age but seem to be most frequent in the third decade, usually postdating the onset of the skin condition by ten or

more years. They are said to have a premature nuclear sclerosis which may contraindicate linear extraction as a method of treatment.

Although the etiology of the skin condition and the cataracts that may ensue is obscure, there can be little doubt that the psychic element plays an important part in it; in fact, this association seems to be a very good example of a true psychosomatic disease. The operative treatment of the patients presents little difficulty, but their psychic instability predisposes them to sudden relapses of the skin condition under the stress of an impending operation. In addition, the skin is very apt to be secondarily infected with pyogenic organisms resistant to antibiotics. To obtain sterile cultures before operation may be almost impossible, so that a decision to proceed in the presence of pathogenic organisms must often be taken. Major postoperative complications are fairly common, having occurred in 36 per cent of all the reported cases summarized by Coles and Laval. Retinal detachment was found in 22 per cent of these. Very severe hypopyon iritis, severe uveitis, possibly of a phacoanaphylactic nature, and retinal bleeding have also been reported, though less frequently.

Psychic difficulties were notably present in 2 of 3 patients seen at Moorfields Hospital. One, a 23-year-old man, twice went into shock while awaiting operation, so that the intervention finally had to be performed by stealth. The second, a woman who had bilateral cataracts, had previously had psychiatric treatment and a leukotomy because of compulsive scratching. Both her skin condition and her mental status improved remarkably, however, after her vision was restored by right and left extracapsular extractions. No family history was obtained in the case of the third patient, a 37-year-old woman, who had had a skin rash for eight or nine years and whose vision had become impaired a few months before she sought advice.

Comment: This syndrome is not too uncommon. There is no question that the anxiety of the patient caused by anticipation of surgery may cause a severe relapse of the skin condition. This complication can frequently be relieved by the use of corticosteroids and, in the reviewer's experience, this has not led to any serious postoperative complications. Antibiotics should be given prophylactically preoperatively and continued postoperatively. The type of extraction will depend to some extent on the age of the patient and the preference of the surgeon. In the younger patients, the zonule may be very firm and an intracapsular extraction may be very difficult. One should always remember that a planned extracapsular extraction is better than an unintentional extracapsular extraction.

P. Robb McDonald

NEUROLOGY

SYMPOSIUM: DISEASES OF THE OPTIC NERVE

FRANK D. CARROLL, JOHN W. HENDERSON, LORENZ E. ZIMMERMAN, FRANK B. WALSH AND C. WILBUR RUCKER

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(One of the features of the Academy meeting each year is the Symposium in which outstanding clinicians present authoritative opinion concerning a subject in which they have had a special interest and talent. The following Symposium was presented at the 1955 meeting. Ed.)

In preparing for this symposium on diseases of the optic nerve, the members of the panel agreed on the following simple terminology: (1) The term optic neuritis refers to the involvement of any part of the optic nerve by a disease process, whether inflammatory, vascular, or degenerative, which impairs nerve conductivity as indicated by visual field changes. When the disease affects the retrobulbar part of the nerve, it is called retrobulbar neuritis; when it affects the papilla, it is called papillitis; and when it affects the papilla and surrounding retina, it is called neuroretinitis. Papilledema, as its name implies, is merely an edema of the papilla; in its early stage it produces only an enlargement of the blind spot. Papilledema and papillitis have the same appearance ophthalmoscopically, but can usually be differentiated without difficulty by means of visual field studies. (2) Optic atrophy is the term used clinically to indicate a permanent loss of part or all of the function of the nerve. Since all optic atrophy is secondary to some disease process, the terms "primary" and "secondary" seem inappropriate. It may be noted, however, that if an active process has involved the disc the ophthalmoscopic picture commonly referred to as "secondary optic atrophy" may or may not result; when it does, the term is perhaps useful. Optic atrophy due to glaucoma or retinal disease will not be considered in this symposium.

The three essentials on which a sound understanding of optic nerve disease must be based are (1) anatomy and physiology, (2) pathology, and (3) visual field changes.

Discussing the first of these, John W. Henderson, Ann Arbor, Michigan, pointed out the fact that the optic nerve, which transmits a sensory stimulus to the thalamus for relay to the cortex, is not a true peripheral nerve but rather a fiber tract of the central nervous system, comparable in many ways to the ascending sensory fiber tracts of the spinal cord and brain stem. Like them, its fibers have no neurilemmal sheath; it lacks the specialized connective tissue framework of cerebrospinal nerves, and it possesses the characteristic glial framework of other white matter of the cerebrospinal axis. In its total course from globe to optic chiasm, it is about 5 cm. in length, subdivided as follows: intracranial, average 10 mm.; intracanalicular, 6 mm.; intraorbital, 30 mm.; and intraocular, 0.7 mm.

The blood supply of the optic nerve is furnished by a fine network of pial vessels which enter the periphery of the nerve to form the dividing septa. The thickness of each septum is proportional to the size of the contained vessel, and the nerve fibers are divided into fascicles by the septal system. All divisions of the nerve except the intracranial portion are supplied by branches of the ophthalmic artery. The intraocular portion of the nerve is fed by branches of the arterial circle of Zinn, as well as by branches of the central retinal artery. Recent injection experiments show a free anastomosis between these two vascular supplies in the region of the lamina cribrosa. The orbital portion of the nerve appears to have a dual arterial supply. The outer pial network penetrates the periphery of the nerve, and a system of axial vessels supplies the core of the nerve. Whether anastomoses exist between these two systems is still in doubt. Normal variations in vascular supply in this as in other parts of the body may explain the varying opinions held by workers who have studied the source and composition of the axial vessels. In contrast to the limited vascular supply apparently available for the papillomacular bundle, the outer pial network of the optic nerve has a rich arterial circulation by way of the ophthalmic artery, with collateral circulation from many internal and external carotid branches, including the anastomosis between the lacrimal and middle meningeal arteries. Whether the axial system continues into the intracanalicular and intracranial optic nerve is not yet certain. One authority states that the intracanalicular part of the nerve is supplied by the ophthalmic artery, but that the pial network is poorer. Many and various adjacent branches supply the chiasm and the intracranial optic nerve. It seems reasonable to infer that the involvement or sparing of the papillomacular bundle in various diseases may be related to the peculiarities of the blood supply.

Since many patients with optic neuritis exhibit a central scotoma, the fibers from the macula are very important to this discussion. Carrying impulses from the macular area, the papillomacular bundle occupies the temporal third of the nerve head and remains in this position in the nerve as it emerges from the globe. It gradually moves to the core of the nerve in its course toward the optic foramen; just as it enters the chiasm, it is found in the exact center of the nerve. The mode and site of passage of the central retinal vessels across the sheaths of the optic nerve may also have important clinical implications. The central retinal artery crosses directly through the vaginal space to enter the nerve, but the vein has a variable course, crossing directly in about half the cases and having a more prolonged intravaginal course in the other half. This exposes the relatively distensible vein to compression from increased cerebrospinal fluid pressure in the subarachnoid space and is thought to be a major factor in the production of papilledema associated with increased intracranial pressure.

The site of the lesion in relation to the point of entrance of the central retinal vessels into the optic nerve probably determines whether or not early visible swelling will occur in the optic disk. Lesions distal to such entrance are said to produce swelling in the nerve head, while those behind this point produce no recognizable fundus changes in their acute phase.

The optic nerve contains visual fibers, pupillomotor fibers, and efferent fibers

which are thought to be vasomotor in function. It behaves like other sensory nerves and conducts visual stimuli in one direction—toward the primary optic centers. Each nerve fiber acts according to the all-or-none principle, and the presence of oxygen is necessary, so that interference with the circulation results in an immediate block of impulses.

Clinically, optic neuritis is evidenced by visual loss, defects in the visual field, pain in or behind the eye on ocular movement or palpation of the globe, decreased pupillary light reaction, and ophthalmoscopic changes.

Describing the histology and general pathology of the optic nerve, Lorenz E. Zimmerman, Washington, D. C., said that the essential components of its relatively simple structure are (1) the partially myelinated nerve fibers; (2) the interstitial cells, which include oligodendrocytes, astrocytes, and microglia; and (3) the fibrovascular septums of pia mater which subdivide the nerve into bundles of nerve fibers. The nerve fiber has two principal components, an axis cylinder and a myelin sheath. Two of the three types of supporting cells, the oligodendrocytes and the astrocytes, are derived from the neuroectoderm and are referred to as neuroglia. The third or microglia cell type is the reticuloendothelial representative and is probably of mesodermal origin. Oligodendrocytes are concerned with the metabolism of myelin. Although they correspond to the Schwann cells of true peripheral nerves, they lack regenerative capacity, so that irreparable damage is done by pathologic processes that destroy both the oligodendrocytes and the myelin sheaths. Astrocytes furnish structural and nutritional reinforcement to the nerve. Microglia are usually present in small numbers, but become very numerous within short periods after many kinds of damage. They possess phagocytic capacities in common with macrophages elsewhere in the body. The pial tissue that subdivides the nerve is exceedingly delicate in the normal nerve, particularly in young persons; later, however, the collagen fibers become coarser and more abundant, forming a thicker connective tissue sheath around the septal vessels, which may interfere with the exchange of oxygen and nutrients in old age.

Tissue fluids are thought to flow backward from the eye through the papilla into the nerve. Any change in the relation of the pressure within the eye to that within the nerve sheaths, causing a diminished flow from the eye into the nerve will favor swelling of the papilla. Enlargement of the blind spot due to papilledema is effected by three mechanisms: displacement, compression, and separation of the retina about the disk. Most important is displacement of retinal tissue away from the disk margins. When papilledema is prolonged, secondary degenerative changes may appear. One of the most readily recognizable of these is the proliferation of fibrous astrocytes. Since it is believed that nerve-fiber degeneration is a stimulus to astrocytosis, pronounced gliosis in an edematous nerve head may be taken as evidence that the nerve fibers have been damaged.

From the viewpoint of the pathologist, the most common type of optic neuritis is that secondary to processes affecting adjacent structures. These are principally infections or tumors of the eye, orbit, bony canal, paranasal sinuses, or meninges. Optic atrophy, which implies both reduction in size and decrease in function,

may be the end result of a wide variety of lesions. When the primary lesion is in the eye, the atrophy is referred to as "ascending;" when the lesion is within the cranium or in the orbital segment of the nerve, the atrophy is called "descending." The ophthalmoscopic appearance of the disk in optic atrophy depends upon a number of factors, the more important of which are the secondary proliferative changes found in the neuroglia, blood vessels, and fibroblasts. In descending atrophy, there is a slow orderly replacement of nerve fibers by astrocytes leading to the picture of simple (so-called primary) optic atrophy. Papillitis, on the other hand, may be followed by a more haphazard astrocytosis with a striking mesodermal reaction ultimately producing the picture of secondary optic atrophy. Finally, in cavernous atrophy the nerve fibers are replaced neither by glial nor by mesodermal connective tissue but by fluid. Escape of the fluid leaves cavernous spaces in the nerve—hence the name.

Optic nerve disease may be caused by any one of the following disorders: inflammation in adjacent structures, systemic infection, multiple sclerosis and allied diseases, hereditary affections, circulatory disorders, trauma, generalized noninfectious diseases, malnutrition, toxicity, tumors, and various unknown conditions.

Summarizing what is known about the first two of these, John W. Henderson said that inflammation extending to the optic nerve may be either intraocular, intraorbital, intracanalicular, or intracranial. Intraocular inflammation invariably produces some degree of swelling of the nerve head when it extends to the optic nerve. Direct extension of retinal or choroidal inflammation leads to a field defect of the nerve-fiber bundle type. Swelling of the nerve head accompanied by a central scotoma occurs in anterior uveitis, and an association of central visual loss and iridocyclitis in the same eye without visible macular or disk change suggests retrobulbar neuritis. Intraorbital inflammation resulting in optic neuritis may be due to pyogenic infections of the face, metastatic infection, or mucormycosis; more often, purulent paranasal sinusitis is responsible. The presence of orbital cellulitis usually establishes the etiological connection between a frankly suppurative sinus infection and optic neuritis; in milder cases, however, in which the clinical picture of optic neuritis is associated with localized sinus infection, attempts to relate the two are seldom justified. Within the optic canal, osteitis may extend to the nerve and produce eventual optic atrophy. Intracranial involvement usually results from an inward extension of inflammation affecting the meninges. The usual lesion is a perineuritis, and peripheral contraction is usually found in the visual fields.

Optic nerve involvement has been reported as an incidental complication in infections of almost all kinds, but whether its occurrence in the course of a systemic infection is directly due to the infective agent or is a part of a toxic encephalomyelitis is difficult to determine. Among the bacterial infections, typhoid fever is said to cause optic neuritis more frequently than any other disease. Apart from certain viral infections considered under the heading of the demyelinating diseases, optic neuritis has been found in association with herpes zoster ophthalmicus and influenza. Its occurrence in infectious mononucleosis,

which is presumed to be viral in origin, has been definitely established, but its true incidence in this condition is not known, because in many cases the eyes are not adequately examined. Among the parasitic infections, malaria sometimes leads to optic neuritis, but visual loss in such cases must be carefully differentiated from quinine amblyopia. Finally, mycotic infections of various kinds may affect the optic nerve to a greater or lesser degree.

Syphilitic disease of the optic nerve, described by Frank B. Walsh, Baltimore, Maryland, may take the form of perioptic neuritis; optic neuritis; and neuroretinitis. Neuritis papulosa, juxtapapillary chorioretinitis, and gumma of the optic disk rarely occur, but when they do, they are difficult to differentiate. Choked disks, which may be present in either congenital or acquired syphilis, are due in 90 per cent of cases to syphilitic meningitis. Vision is good, but atrophy of the nerves may supervene. Intensive treatment undoubtedly improves the outlook for patients with syphilitic parenchymatous (primary) atrophy; if a patient is not blind within three years from the onset of the atrophy, the ultimate outcome should be reasonably favorable. The outlook for retaining or regaining normal vision in cases of secondary atrophy in which syphilitic meningitis is associated with optic neuritis or papilledema and the retinal vessels are narrowed is not good.

In discussing the demyelinating diseases, C. Wilbur Rucker said that the similarities between them are due, at least in part, to the fact that the number of ways in which the tissues of the central nervous system can react to noxious agents is limited. Diseases of this class, which includes multiple sclerosis, optic neuromyelitis, progressive subcortical encephalopathy, and postinfectious encephalitis, differ greatly in the location and severity of the lesions, in the course of the disease, and probably in their causes. All of them, however, are characterized by loss of myelin sheaths, and all affect vision in one way or another. Certain anatomical features by which they may be differentiated from one another were pointed out by Lorenz E. Zimmerman. In multiple sclerosis, the differential histopathologic features are minimal necrosis and axonal degeneration accompanied by mild mesodermal and microglial reaction. Neuromyelitis optica is characterized by marked necrosis of nerve fibers and intense microglial response; in diffuse sclerosis, there are varying degrees of necrosis and a tendency to cyst formation; and postinfectious or postvaccination encephalomyelitis is associated with a striking perivenous distribution of lesions and an especially intense inflammatory response.

Frank D. Carroll expressed the belief that one of the most frequently overlooked causes of optic neuritis is hereditary disease. The symptoms, signs, and early course of hereditary optic atrophy are the same as those of retrobulbar neuritis or papillitis due to other causes. There is great variability in the degree of final vision: in the same family, some may have vision as good as 20/30 but most will have 20/200 or less. Total blindness is very rare.

Disease of the nutrient arteries of the optic nerves as an occasional cause of loss of vision was discussed by C. Wilbur Rucker. Senile atherosclerosis, arterial hypertension, and several varieties of inflammation of the walls of the arteries,

including temporal arteritis, may lead to partial or complete occlusion of the central retinal artery or one of its branches; in other cases, ischemic changes may be produced. Temporal arteritis, when it impairs vision, becomes a medical emergency, for when one eye is affected the other is apt to be also, with the result that the patient becomes completely blind. The most effective therapeutic agent now available is cortisone administered systemically. Further loss of vision seldom ensues after its administration is begun and the second eye almost never becomes affected.

Trauma to the optic nerve, according to Frank B. Walsh, may result in its avulsion; in partial or complete division; or in direct injury without division associated with pressure or fracture. Trauma may also cause indirect injury to the optic nerve and unusual injuries sometimes result from such traumatizing circumstances as electrical shock, operations on the nose and lacrimal sac, and orbital injections of anesthetic agents.

The problem of optic nerve involvement in generalized noninfectious diseases due to blood dyscrasias, blood loss, allergy, metabolic dysfunction, inherited systemic disease, and nutritional deficiency was discussed by John W. Henderson. Frank D. Carroll described the visual impairment brought about by malnutrition, which was common in Japanese and North Korean prison camps, and by various toxic agents, some 50 of which are described in detail.

The differential diagnosis of tumors of the optic nerves and chiasm was dealt with by Frank B. Walsh, who said that with the exception of metastatic tumors, all those that affect these structures, whether intrinsic or extrinsic, require surgical investigation and in most cases removal. Roentgen therapy, however, should be used in certain instances, as when glioma invades the chiasm, because in this case surgical removal is contraindicated.

Finally, C. Wilbur Rucker pointed out the fact that the prognosis in optic neuritis of unknown origin is generally favorable, with nearly three-fourths of the younger patients regaining good vision.

ALTITUDINAL (HORIZONTAL) HEMIANOPSIA

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Rev. oto-neuro-oftal. y de cir. neurol., 1955, *30:* 40–49

Homonymous altitudinal hemianopsia consists of blindness for either the upper or the lower half of the visual field of one or both eyes. The blind area is limited by a horizontal line which bisects the macula. The name is also given to hemianopsia, even if it is not complete in its respective field and with partition of the macula, and also to incomplete hemianopsia of the visual field of either or both

eyes even with a central scotoma. The field defect involving the upper half in one eye and the lower half in the other eye is called crossed or alternate hemianopsia. Altitudinal hemianopsia of the upper visual field is less frequent than inferior hemianopsia. Its horizontal limiting line is never rectilinear, but undulating, often in accordance with defects situated on the horizontal meridian. The field defects which are due to inflammation or degeneration of the retina, optic nerves and chiasma are incongruous and as a rule, they develop in association with central scotoma of varied size and intensity. Hemianopsia caused by retrochiasmal lesions, is always congruous.

The causal factors of altitudinal hemianopsia, in order of frequency are as follows: Opticochiasmal arachnoiditis, vascular changes, hemorrhage, embolism, aneurysm and atheromatous diseases, trauma, infections, ocular diseases (glaucoma and retinopathies), cerebral diseases (tumors, oxycephaly and acromegaly), and anemia. Vascular retinopathies, atrophy of the optic nerve, chiasmal and intrachiasmal tumors, compression of the nerve, and aneurysm of the ophthalmic artery are also very important causal factors of altitudinal hemianopsia.

The authors describe, by means of perimetric graphs, the type and evolution of altitudinal hemianopsia in 24 cases observed by them. Altitudinal hemianopsia in these cases was due to a retinal lesion in 6 cases, diseases of the optic nerve in 2 cases, tumoral compression of the optic nerve in 1 case, arachnoiditis in 9 cases, astrocytoma of the cerebellum in 1 case and lesion of the arteries of the cuneus, embolism to the posterior temporoccipital arteries and tumor of the thalamus involving the thalamus and the internal capsule in 1 case each. The causal retinal lesions in 6 patients were glaucoma, bilateral detatchment of the retina as a result of lesion of the retinal blood vessels, retinopathy due either to hypertension or to diabetes, angiosclerosis and embolism of the upper branch of the central retinal artery.

In 1 patient incongruous, incomplete, alternate, horizontal hemianopsia was due to tabes. It developed in three years into lower hemianopsia with scotoma. Another patient had optic neuritis or papillitis, probably of viral origin. There was retinal edema. An operation for intracranial decompression resulted in cure of the patient. A post-traumatic lesion causing hemianopsia was associated with cranial fracture in 2 patients. In one case a lesion of the optic nerve was located on the segment of the nerve which enters through the lower border of the chiasm causing compression of the upper fibers of the optic nerve. In another hemianopsia of the left eye with scotoma was due to direct compression of the optic nerve, by pressure upon the upper fibers of the nerve, by a tumor.

The 9 patients with arachnoiditis showed several field alterations with great lack of congruence and great diminution of visual acuity in all cases. In some of the patients, the line of division of hemianopsia was located exactly over the meridian.

In 1 patient there was hydrocephalus due to astrocytoma of the cerebellum. Hemianopsia was due to pressure by the third ventricle which was greatly dilated and tense, upon the anterior surfaces of the optic disk, near the chiasm with compression of the optic disk against the Willis' circle. A complete lower altitudinal

hemianopsia occurred because of a lesion of the arteries of the cuneus. One patient had altitudinal hemianopsia with certain non-typical characters for all the isopters. The patient had a normal visual field before an operation which consisted of removal of a large left postcentral parasaggital meningioma (150 gm. in weight). After the operation the patient observed the loss of vision from hemianopsia with scotoma in the upper field.

The mechanism of production of horizontal hemianopsia is complicated and is in accordance with the etiology and location of the lesion in each case. Each case deserves special consideration and discussion by itself. Altitudinal hemianopsia due to retinal, chiasmatic or retrochiasmatic lesions as a rule produce atrophy of the optic tract, especially the chiasmatic lesions. Lesions of the optic nerve caused by trauma of the optic nerve with partial lesion of the nervous fibers and without functional changes in the remaining non-traumatized fibers constitute the exception to the rule. Hemianopsia caused by opticochiasmatic arachnoiditis produces blindness in all cases without exception. Hemianopsia due to trauma in the head or to bullet wounds do not progress after the resulting nervous lesion is stabilized. If the patient recovers from the wound, the residual damage does not progress. The prognosis of hemianopsia caused by tumors depends on the extent to which the compression or displacement caused by the tumor can be relieved by surgical treatment.

SPONTANEOUS HEMATOMA OF THE CEREBELLUM AND HEMATOMA OF THE FOURTH VENTRICLE

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Spontaneous hemorrhage of the cerebellum and the consequent cerebellar hematoma have distinct symptoms which enable the neurosurgeon to reach a diagnosis with certainty and to perform a life-saving neurologic operation. The diagnosis, however, is rarely made. When the stroke of the cerebellar hemorrhage is severe, acute dizziness, unconsciousness, deep coma, and death occur in rapid succession. The hemorrhage in this case is a necropsy finding. On the other hand, when the stroke is not very severe and is overlooked while a tumor of the cerebellum or of the posterior fossa is suspected because of the symptoms of intracranial hypertension, the hematoma is found during the operation. There is no pathognomonic sign of cerebellar hemorrhage, but both it and the hematoma can be diagnosed when the hemorrhage is moderate or small. The symptoms of cerebellar hemorrhage consist of the occurrence of a sudden stroke in which the patient falls to the floor unconscious and with acute vertigo. This is followed by the establishment of a unilateral cerebellar syndrome (acute constant dizziness,

nystagmus and rightward lateral pulsion). This syndrome is not accompanied by symptoms showing lesion of the long nervous routes (hemiparesis or hemianesthesia) and the cerebral nerves are not involved. The differential diagnosis must include other diseases which cause sudden attack of acute dizziness and the unilateral cerebellar syndrome; namely, the Wallenberg's syndrome, Mènière's syndrome, tumors of the pontocerebellar angle, and thrombosis of a cerebellar artery.

Once a diagnosis of a vascular hemorrhagic lesion of the cerebellum has been made, the diagnosis of cerebellar hematoma is simple. If the symptoms of the cerebellar syndrome grow worse, the presence of hematoma is obvious. Prompt surgical evacuation of the hematoma results in cure of the patient. Prior to the operation, however, it is advisable to perform a ventriculography with lipiodol, for exact diagnosis. This procedure is especially indicated in cases showing atypical signs of hematoma. Lipiodol ventriculography will show, in almost all cases, the dilatation of the fourth ventricle by the hematoma.

The causes of cerebellar hemorrhage are the same as those of cerebral hemorrhage, mainly essential or secondary hypertension. However, young persons with normal blood pressure and without syphilis, diabetes or infections often have a cerebral or cerebellar hemorrhage. The cause of such hemorrhages is unknown, but it is possible that the vascular lesion which produces the hemorrhage is hidden in the area of destruction caused by the hematoma. The author reports a case with clinical observations and a necropsy. A woman, 39 years old, had three (probably four) sudden strokes of cerebellar and meningeal hemorrhage. She had been amenorrheic since the age of 27 years. Her blood pressure was normal. She did not have arteriosclerosis, syphilis, diabetes or renal disorders. The attacks occurred in September and November 1953 and in April and probably in July 1954. Both the attacks and the consequent unilateral cerebellar syndrome followed the pattern previously described for cerebellar hemorrhage, but the syndrome was somewhat distorted by the presence of signs showing involvement of certain cerebral nerves and the lack of edema of the papilla. The cerebrospinal fluid obtained by lumbar puncture was normal after the third attack, but was hemorrhagic after the suspected attack in July 1954 and twice again in the course of the final period of the disease.

During the final period of the disease, occipital headache, hypersomnia, and rigidity of the nucha became acute and bilateral paralysis of the third pair of cerebral nerves and left hemiparesis appeared. The patient died suddenly from a syncope. A definite diagnosis was never made. Necropsy showed cerebellar hemorrhage and an enormous well encapsulated hematoma in the fourth ventricle, which caused dilatation of the ventricle and chronic pressure and deformation of the bulb. The authors believe that the first two strokes were caused by functional spasmodic anoxia. The true hemorrhage was that which occurred in April 1954. It was immediately followed by hematoma formation. Blood reached the meninges only some time after the hemorrhagic stroke. The patient had endocrine disorders, which may have affected the vascular tree of the cerebellum, resulting in the cerebellar hemorrhage.

OCULAR MUSCLES

HEAD TILTING IN THE DIAGNOSIS OF OCULAR MUSCLE DISTURBANCES

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J. Internat. Coll. Surgeons, 1956, *25:* 590–594

Ocular torticollis may be defined as an abnormal position of the head caused by a disturbance of ocular motility, usually a form of paralysis of the vertically acting muscles. The condition is variously referred to as head tipping, head tilting, abnormal head posture, or corrective posture. Occasionally the abnormal head position may be the predominating feature of squint, especially in children. Its presence is always of great significance in the consideration of surgical treatment of the ocular muscles. Abnormal head posture in ocular muscle paralysis of congenital origin is generally accompanied by scoliosis and usually exists without the patient's being aware of it. It is adopted in compensation in the absence of obtrusive diplopia (alternation). When the paralytic squint is acquired, the patient is aware of his head posture and assumes the position in an attempt to overcome diplopia; there are no anatomic changes in the structure of the vertebrae or their attachments. It is sometimes seen in concomitant squint in older patients, also, in whom it was most probably of paralytic nature in early infancy.

Most vicarious rotations of the head of ocular origin can be subdivided into various components. Diplopia, the most annoying symptom of paralytic squint, will determine in large part the abnormal head posture. Horizontal diplopia, crossed or uncrossed, may be minimized by turning of the head to one side or the other. Vertical diplopia may be lessened by elevation or depression of the chin. Torsional diplopia may be decreased by tipping of the head toward one shoulder.

The simplest situation is that of paralysis of a horizontally acting muscle, which results in the turning of the face toward the field of action of the paralyzed muscle. Turning toward the right is suggestive of paralysis of a right-hand rotator, either the right lateral rectus or the left medial rectus, and turning toward the left, either the right medial rectus or the left lateral rectus. Long-standing paralysis may be accompanied by contracture of the direct antagonist, in which case mere rotation of the face will no longer suffice to eliminate horizontal diplopia. Because raising of the eyes causes relative convergence, elevation or depression of the chin may be adopted. In the case of right lateral rectus palsy, for example, with the face turned toward the right, esotropia may be further reduced by lowering the chin; and in a case of left medial rectus palsy exotropia may be minimized by turning the face to the right and raising the chin.

Postural changes considered in relation to the vertically acting muscles present

a more complicated problem, because these muscles have component actions in more than one direction; they act not only as elevators and depressors, but also as horizontal rotators and in a torsional capacity (the principal action of the obliques). Generally, however, it may be said that in patients with paralysis of an elevator the chin is elevated, and in those with paralysis of a depressor the chin is depressed. Considerable variation may be found in the head posture of patients with paralysis of the superior rectus, depending on the amount and type of diplopia and on the fixing eye. If the nonparetic eye fixes, the chin is elevated, the face turned to the ipsilateral side, and the head tipped to the contralateral shoulder. On the other hand, if the paretic eye fixes, the chin is raised, the face turned to the paralytic side, and the head tipped to the shoulder on the paralytic side. When ocular torticollis is the predominating feature, the latter condition usually prevails.

In superior oblique palsy, on the other hand, the muscle that would normally cause depression, abduction, and intorsion, permits the eye to be elevated, adducted, and turned outward. Tipping of the head to the nonparalyzed side is the characteristic posture in paralysis of this kind, but if the head is forcibly tipped to the paralyzed side, in right superior oblique paralysis, for example, the ipsilateral or right superior rectus, when attempting to overcome extorsion, may cause elevation of the ipsilateral or right eye (as in the Bielschowsky test). In contrast, if an eye with a paralytic superior oblique is used for fixation (secondary deviation), tipping of the head to the ipsilateral side is the rule. For example, if the right superior oblique is paralyzed and the right eye fixes, overaction of the contralateral yoke muscle, the left inferior rectus, will be encountered. This produces left extorsion and can be overcome by tipping the head to the right shoulder, that is, by placing the eyes in left cycloversion.

Similarly, primary paralysis of the inferior rectus may be found to produce a head tilt to the normal side with turning of the face to the affected side and depression of the chin. Here, however, the head tipping is probably due more to the torsional diplopia of the overacting antagonist, the ipsilateral superior oblique, than to the effect of the paralytic inferior rectus. Paralysis of the inferior oblique is extremely rare, but when present is accompanied by tilting of the head to the ipsilateral side, elevation of the chin, and turning of the face to the normal side. In multiple paralyses, that is, when more than one muscle is involved simultaneously, either in the same or in both eyes, the patient chooses a position allowing binocular single vision with the greatest relief to the paralyzed muscles. Head posture affords little practical help in the analysis of these cases. Differentiation between ordinary and ocular torticollis is facilitated when it is remembered that in ocular torticollis there is no cervical pathology and the head can be straightened, although when it is, diplopia or suppression results; conjugate movements of the eyes are abnormal and ocular muscle imbalance is typical.

Valuable as the various postural changes associated with the oculomotor paralyses are in enabling the ophthalmologist to arrive at an accurate diagnosis, they should be regarded as diagnostic aids and not as substitutes for time-tested procedures.

THE ORBIT

CHRONIC ORBITAL MYOSITIS

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Bull. Soc. Belge d'Ophtal., 1955, *110:* 276–294

Unilateral exophthalmos without signs of reaction in the conjunctiva or the eyelids, though usually due to an orbital tumor, may be caused by inflammatory pseudotumors or by chronic orbital myositis. Orbital myositis may be either a congenital or an acquired degenerative condition, or part of an acute inflammatory process affecting the eyeball or the orbit, or a chronic condition. The chronic form of the disease is rare, and it has even been said that it does not exist except in association with a diffuse orbital cellulitis. The histopathologic findings in three new cases observed by the authors, however, showed no orbital tissue lesions apart from the muscular changes; in particular, there were no signs of any venous injury. Chronic orbital myositis should unquestionably be regarded as a distinct entity characterized essentially by an inflammatory hypertrophy of one or more ocular muscles, all the other orbital tissues remaining intact. The infiltration of these tissues when compared with the muscular lesions is so slight that it can only represent a reaction to the muscular inflammation.

The histopathologic lesions of chronic orbital myositis are identical with those found in the malignant exophthalmos of Basedow's disease (exophthalmic ophthalmoplegia or thyrotropic exophthalmos). Side by side with ordinary or thyrotoxic exophthalmos, the anatomical substratum of which consists especially of an increase of fatty deposits and which is accompanied by general symptoms characteristic of thyroid intoxication, there exists a severe exophthalmos with histological lesions of a hypertrophic and inflammatory type localized almost exclusively in the orbital muscles. Moreover, it is known that thyrotropic exophthalmos, though often bilateral, may be unilateral or may be strongly predominant on one side. In addition, the symptoms of hyperthyroidism may have disappeared at the time the exophthalmos appears, and in fact the exophthalmos may occur after surgical or even medical treatment of the disease. Signs of hypophyseal hyperfunction are often present, and it is almost always possible to detect a characteristic symptom: hypertony with retraction of the upper eyelid. Again, there are cases of thyrotropic exophthalmos in which no manifest signs of endocrine dysfunction can be detected, so that some authors consider all cases of chronic orbital myositis to be dependent on thyrotropism.

Chronic orbital myositis may, therefore, constitute a special clinical syndrome of "tumoral exophthalmos without a tumor," without extraorbital participation, and even without general signs of endocrine disturbance or any other causal condition.

Unfortunately, it is often impossible to differentiate between a pseudotumor caused by orbital myositis and a genuine orbital tumor on the basis of the clinical symptoms alone. Recognition of the condition on ophthalmological examination must therefore be relied on to save the patient from an unnecessary exenteration, if not from loss of vision in the affected eye. In any case, when a clear-cut diagnosis cannot be made, exenteration should not be undertaken without a preliminary orbitotomy with exploration of the orbital contents and biopsy. This procedure, however, should be avoided whenever possible, because it leads to exacerbation of the symptoms, increases edema, sometimes permanently, and may even result in functional loss of the eye.

Comment: In this article the authors have recorded their clinical, surgical, and histopathologic observations on 3 cases of an infrequently reported disease process. Case reports prior to this one have appeared not only under the title that the authors have employed but also under titles such as "pseudotumor" and "exophthalmic ophthalmoplegia." In the literature of more recent years there may be isolated cases of "chronic orbital myositis" included in reports describing the severer examples of the "hyperophthalmopathy of Graves' disease." Even with this wide choice of terminology, I would estimate that there are less than two dozen clear-cut examples of this disease reported in the literature.

Among the observers who have reported cases of "chronic orbital myositis" there is general agreement that the disorder is (1) definitely an inflammatory process; (2) it is chronic and progressive; (3) the predominant clinical findings involve the extraocular muscles with secondary exophthalmos of the affected eye; (4) there are marked similarities between the histologic picture of this disorder and that noted in malignant exophthalmos of Graves' disease; (5) it constitutes a definite clinical and pathologic entity, and (6) its cause is unknown. Beyond this point some discrepancies begin to appear as to what the disease really is.

The main point of difference among the various observers revolves around the histologic picture. Some have regarded the typical finding as represented by a lymphocytic infiltration, whereas in the authors' cases a fatty infiltration of the muscle was considered characteristic. Other terms such as "fibrosis," "hypertrophy," "degeneration," and "all degrees of muscular dystrophy" have been used by various observers to describe the histologic picture. Whereas some (such as the authors) contend that the disease is strictly confined to the extraocular muscles, others have felt that the change within the muscle fibers was but the dominant finding in an inflammatory condition that involved other components of the soft tissues within the orbit.

In my own experience I have noted cases such as the authors' among people undergoing either an orbital exploration for neoplasm or an orbital decompression for so-called "malignant exophthalmos." Indeed, on the basis of this experience, I am willing to go one step further than other observers by stating that malignant exophthalmos and chronic orbital myositis are not only "similar" but are probably the same disease with slight variations in the histologic picture from case to case. By this statement I do not mean to leave the impression that the disorder should be called malignant exophthalmos or any other term in preference to chronic orbital myositis, but only to caution those who are prone to regard the disease under discussion as a separate clinical and pathologic entity. Until more is known about the histologic picture of these closely allied inflammatory processes within the orbit, I hesitate to advocate the premise that an inflammatory process more predominant in one soft tissue component of the orbit as compared to another should constitute a separate disease entity.

This brings to mind the increasing interest in the problem of pseudotumor (this term used in its broadest sense to include the several inflammatory diseases that are difficult to differentiate from orbital neoplasms) of the orbit that has come about since the antibiotics nearly wiped out the old-style orbital cellulitis due to bacterial and allied invaders. There is a great need at present for some pathologist to collect a number of histologic specimens of this and related diseases and correlate them with the observations that have been made by ophthalmologists familiar with the various clinical manifestations of pseudotumor.

For those who might be interested in a report in the English language similar to the above, the reader is referred to the publication of Dunnington and Berke, Arch. Ophth. 1943, *30:* 446.

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TRABECULAR MESHWORK

Ashton, Brini and Smith (Brit. J. Ophth., 1956, *40:* 257–282) suggest that recent trends in research on glaucoma necessitate a precise knowledge of the anatomy of the uveoscleral trabecular meshwork.

The present study consisted of the examination of the trabecular meshwork of the human eye, by histologic sections in three different planes and by flat preparations of fresh specimens. The material used included postmortem specimens and eyes removed for malignant melanoma of the choroid.

The findings in the main confirm the work of previous authors:

(1) The meshwork may be divided into an inner uveal part (containing outer and inner components) and an outer scleral part, but further definite subdivisions are not yet readily demonstrable.

(2) The shape and orientation of the fibers appear to vary according to the plane of the section; anteroposterior sections show short rods, while circumferential sections show longer rods disposed circumferentially. It is concluded, therefore, that the arrangement is that of circumferentially disposed flattened bands, each perforated by oval stomata, the anteroposterior sections giving cross sections of the bands and hence appearing as rods. This conception is supported by flat sections and flat preparations.

The existence of pores in the inner wall of Schlemm's canal connecting with the inter-trabecular spaces is confirmed.

It is concluded that patent tortuous pathways existing in the trabecular meshwork enable communication between the anterior chamber and Schlemm's canal. No correlation was found between the histologic appearances and the age of the patient.

RETINA AND VITREOUS

DIASTOLIC RETINAL PRESSURE: ITS VALUE AND SIGNIFICANCE IN VASCULAR HYPERTENSION

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Paris

Tr. Ophth. Soc., U. Kingdom, 1955, *75:* 391–403

A number of measurements can be made of the retinal circulation; namely, the diastolic, systolic and mean tensions, Fritz's index of rigidity, and measurements of output and of capillary tension. But among these, the only one that has survived the proof of time is the measurement of diastolic retinal tension proposed by Bailliart more than 30 years ago.

Criticisms may be made of this technique, particularly in the physical arrangement. The instrument used is not of the desired precision, and the eyeball on which this pressure is exerted is far from being a closed cavity with constant tension. Additionally, there are the errors of the observer and the values given by the dynamometer. However, it is well to remember that the majority of authors today are in agreement in recognizing in this method an error of no more than 1.5 mm. of mercury when repeated measurements are made by the same observer.

The major value of these measurements is clinical. The ratio between the diastolic retinal and systemic pressures, or retinal-humeral ratio of Bailliart, is normally almost exactly 0.50. This value varies appreciably in hypertension depending upon the clinical type and the therapeutic measure employed.

Studies were made of 321 patients with hypertension. The results are shown in Table 1.

It is demonstrated that 86 per cent of malignant hypertensives have a high ratio and 72 per cent of the benign hypertensives a low ratio.

In comparing the ratio with Keith-Wagener's classification of fundus disease a close parallelism is found particularly in the fourth terminal stage (of papilloedema, hemorrhages and deposits). (Ed.) But there is no absolute rule for the value of the retinal-humeral ratio according to the anatomical state of the retina. In fact, the low ratios may coincide with advanced retinal lesions and high ratios may accompany the anatomical findings of classically benign indication.

To determine which was the better indicator of malignant hypertension, a comparison was made of the results of tension studies and fundi examinations. The results are shown in Table 2 and indicate the superiority of the retinal-humeral ratio over the fundus examination.

Comment: Determination of the diastolic retinal-humeral tension ratio is an interesting method of examination and may aid in the differential diagnosis of systemic hypertension

TABLE 1

Type of Hypertension	Retinal-Humeral Ratio		
	Less than .50	Exactly .50	More than .50
Malignant	11	10	133
Benign	43	30	29
Potentially malignant	6	6	28
Benign glomerulonephritis	5	6	2
Malignant glomerulonephritis	2	11	1

TABLE 2

Comparison Between Ophthalmoscopic Appearance and Retina-Humeral Ratio in the Prognosis of Malignancy

Type of Hypertension	No. of Cases	Indicative Concordance	Fundus in Prognosis of Malignancy	R.H.R. in Prognosis of Malignancy
Malignant	154	97	4	53
Potentially malignant	40	23	1	16
Glomerulonephritis	25	4	2	7

if the examiner becomes an expert in its use. It harbors, however, the same pitfalls, which made the Keith-Wagener classification of hypertensive fundi occasionally difficult to apply.

It is essential for its correct interpretation to know all of the local conditions which may alter the diastolic pressure in the central artery and thus keep clear the issue of the systemic condition interpreted through it.

A unilateral edema of the disc or a unilateral low diastolic pressure in the central artery, for instance, may lead one observer to suspect an impending occlusion of the central retinal vein, and another to use a mechanical and meaningless application of a classification, such as placing one eye into one category and the other eye into another of a certain classification. Only awareness of the local nature of the condition will prevent diagnostic errors.

Knowledge of the retinal-humeral ratio values, determined repeatedly in the same patient, would be a desirable adjunct to the Keith-Wagener classification. One might get prognostic information earlier by detecting the cause of the arteriolar lesions before they become manifest to the observer's eye, the results of the dynamometric and of the ophthalmoscopic examination having a relationship somewhat like cause and effect.

In this connection a report by Kirby and Hollenhorst (Acta XVII Councilium Ophth. 1954, pp. 335) is of interest. These authors found in 2 hypertensive patients, both of whom had a ligation of one internal carotid artery for an intracranial aneurysm, a much milder degree of hypertensive retinal arteriolar sclerosis coupled with the much lower diastolic pressure in the central retinal artery on the side of the ligation.

These 2 cases throw light upon the limitations of information which may be gained from ocular examination either by means of the ophthalmodynamometer or of the ophthalmoscope.

The somewhat arbitrary assumption that the less affected eye is the true index of the patient's general state and that local conditions, such as an atheroma of the central artery or an impairment of the circulation in the central vein, are responsible for unilateral, more pronounced degrees of vascular lesions may not apply to all cases of asy-

metric fundus lesions. A spontaneous condition similar to that produced by ligation of the internal carotid artery might conceivably be caused by atheromas in this vessel, and it would be interesting to see the results of angiography on the side of the lesser lesions in cases of asymmetrical hypertensive retinal changes.

BERTHA A. KLIEN

IDIOPATHIC RETINAL DETACHMENT

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Am. J. Ophth., 1956, *41:* 660–667

In normal eyes the vitreous adheres to the region of the optic nerve and—more firmly—to the periphery; adhesions between the retina and the vitreous in other parts of the adult human retina, however, are not generally thought to exist. Nevertheless, ophthalmoscopic examination in cases of retinal detachment reveals tiny strands that seem to be pulling small flaps and even isolated pieces of the ruptured retina into the vitreous space. These strands have been described in pathologic specimens as the result of a degenerative or postinflammatory condition of the vitreous body and the retina. Although the suggestion has been made that changes in the retina and the vitreous might strengthen tiny retinovitreous adhesions to such an extent that they would become factors in the development of retinal tears, it does not seem to have been supported by histologic evidence. The discovery of retinovitreous adhesions, apparently congenital in origin, in the enucleated eye of a nine-month-old child with a diagnosis of pseudoglioma (not confirmed on microscopic examination) led to a search for similar adhesions in normal eyes. Eventually, a retinovitreous strand of the same nature as those found in the eye with the congenital anomalies was discovered in the eye of a patient who had died of sprue. With the exception of a few tiny hemorrhages in the retina, the eye was completely normal in all other respects. In some cases of retinal detachment, therefore, congenital microanomalies may be responsible for the retinal tears. Further evidence in support of such an origin for retinal detachment was provided by the case of a 60-year-old man with subjective symptoms suggestive of a posterior detachment of the vitreous body. Ophthalmoscopic examination confirmed the diagnosis and revealed a small round hole, surrounded by tiny hemorrhages, in the equatorial region at the temporal side of the right eye. No other anomalies were found and no traces of a preceding infection or degeneration could be detected. Clearly, therefore, a piece of the retina had been torn out by some force, presumably a pull on the retinovitreous adhesion resulting from retraction of the vitreous.

Idiopathic detachment of the retina of the kind described may be comparatively rare, but the possibility that retinovitreous adhesions of the congenital type, when combined with later degenerative or inflammatory processes, may play an important part in other cases of retinal detachment by providing a framework for the development of the strong strands often associated with retinal tears cannot be disregarded.

Comment: Tiny congenital vitreo-retinal adhesions such as the authors demonstrate histologically in the eyes of two different individuals may not prove to be so rare as they seem at the moment if a systematic search for them on normal eyes is carried out.

Their cellular elements are of ectodermal origin, and the authors ascribe their presence to an early embyonic disturbance of the equilibrium in the share of the ectoderm and mesoderm in the formation of the vitreous.

These adhesions, even if delicate, appear firmly anchored within the deeper layers of the retina; the nuclei of their cellular components can be followed through at least the inner half of the retina. Associated with incidental pathologic conditions of the vitreous, degenerative or inflammatory in nature, they may prove to be stronger and more destructive than vitreo-retinal adhesions fortified by more superficial cellular growth from the fibrogenetic activity of phagocytes and wandering cells (Klien, Am. J. Ophth., 1955, *40:* 515).

Traction upon such a congenital strand by a posterior vitreous detachment in later years could lead to retinoschisis, to internal ruptures of retinal cysts, or to a tearing out of an operculum such as the authors found clinically, all conditions with an inherent danger of retinal separation. This is an important contribution to the pathogenesis of retinal detachment, the degree of importance will depend on the frequency of such microanomalies, which has not yet been ascertained.

BERTHA A. KLIEN

CONGENITAL DISEASE

CONGENITAL CATARACT IN RELATION TO RUBELLA

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Tr. Canad. Ophth. Soc., 1954–55, 7: 131–141

The most striking feature of congenital cataract following maternal rubella is that the cataracts, which are usually bilateral, are obvious from birth in nearly all cases as white opacities completely occupying the pupillary area. Probably the only exceptions occur in the few cases in which there is some temporary clouding of the cornea—in them the cataract may not be detected until the cornea clears.

In the undilated condition of the pupil the opacities fill the entire area. After dilation, they appear densely white—sometimes quite pearly—in the central area with a small, apparently clear zone between this and the pupillary border of the iris. Closer examination reveals in this zone a less dense opacity of smoky appearance, and outside of it there is only a narrow ring through which a red reflex can be obtained. Although the general appearance of the cataracts is much the same in all cases, two main types are identifiable. In one the contrast between the larger, dense, white central area and the smaller, cloudy peripheral zone is very marked. In the other the density of the cataract is more uniform throughout; its stage is intermediate between those of the two portions of the other type.

Various other ocular abnormalities may also appear in children with this condition. In some cases the iris has a somewhat atrophic aspect; of greater importance is the fact that mydriasis is difficult to obtain and to maintain, especially after surgical intervention. Intolerance to atropine is also found in many cases. Definite microphthalmia was evident in a very large proportion of the author's patients. This feature is readily discernible by comparison with the unaffected eye when the condition is unilateral; when it is bilateral, comparison of the measurements of the affected eyes with those found in normal eyes of babies of similar weight and age will be needed to demonstrate its existence. Shallowness of the anterior chamber, nystagmus, peculiar pigmentary changes in the fundus, and hydrophthalmia, seen in a few cases, are diagnostically significant.

The presence of one or more of the associated defects commonly found in this condition, notably deaf-mutism, cardiac anomalies, failure to thrive, mental retardation, and microcephaly, in association with cataract, or with each other in the absence of cataract, is an important part of the syndrome and is therefore extremely valuable from the viewpoint of diagnosis.

The mental retardation found in these children is often attributed to the defective state of the organs of special sense. Defective vision and defective hearing, especially if coexistent, would naturally have an adverse effect on a develop-

ing child, but in many of these children there seems to be mental retardation *per se*; in some cases, unfortunately, it progresses to a state of complete imbecility.

Early interference is not only justified, but necessary, because if the cataract is allowed to persist untreated, nystagmus develops. Among the difficulties that may be encountered by the surgeon are shallowness of the anterior chamber; difficulty in obtaining mydriasis and in maintaining it, especially after operation; difficulty in dealing with the cataract itself; slow absorption after discission and the necessity for repetition of the process; the possibility of secondary glaucoma resulting from adhesions of the iris, lens matter, and vitreous in the anterior chamber; and the fact that the prognosis for vision is poor, because of microphthalmia; the presence of nystagmus and other ocular defects; and mental retardation. Although immediate operation is advisable when both eyes are affected, one eye should be operated on first. If the first operation is successful, the second need not be delayed, but if it is unsuccessful a change in technique or delay may be wise. When cataract is confined to one eye, on the other hand, it seems to be generally agreed that no operation is necessary. Cordes' modification of Barkan's linear extraction with the specific refinements stressed by him can now be considered the operation of choice. In most of the patients, however, the prognosis for useful vision is poor.

The lens is most apt to be affected when the maternal infection occurs before the eighth week; between the eighth and the twelfth weeks, the likelihood of lens injury lessens, and after the twelfth week there is every chance that the lens will escape. The fact that lens changes do not occur after the third month may perhaps be explained by the protection afforded the lens by the lids and by Descemet's and Bowman's membranes after that time.

The diagnosis of the type of cataract seen in an infant and the cause to which it should be attributed is important not only as an indication for the operative procedure to be used and the prognosis, but also as a guide to the advice that should be given the parents in regard to future children of the marriage. Obviously, then, a full and careful history of the maternal pregnancy, especially in the early months, must be elicited, and careful inquiry should be made into any possible hereditary taint. In the examination of the child, the special characteristics of the cataract should be noted, and other abnormalities should be looked for. In unilateral cases, the unaffected eye should also be examined. The absence of the typical retinopathy in that eye does not rule out rubella, but its presence is very suggestive even when the history of rubella is wanting or vague.

Comment: Sir Norman M. Gregg's comment concerning the very frequent accompaniment of associated systemic defects (dear-mutism, cardiac anomalies, mental retardation and microcephaly) with congenital cataract of rubella origin is worthy of careful study by every ophthalmologist. This editor, moreover, has been impressed repeatedly that phenocopies (syndromes resulting from intrauterine infection or inflammation) usually exhibit numerous and extensive systemic anomalies in association with ocular aberration. Consequently no ophthalmic history is complete, particularly when concerned with a sporadic case of congenital ocular disease, until a careful inquiry has been made concern-

ing the maternal health and contacts with infectious disease during the particular pregnancy. There is evidence that the fetus may be deleteriously affected upon exposure or contact of the mother to certain viral diseases even though the mother subsequently exhibited no illness.

The author's point concerning the poor prognosis both for surgical success and resultant visual acuity is also well taken. These patients, in our experience, are poor anesthetic risks (possible liver disease?) and surgical complications are frequent. In these cases it is wise for the ophthalmic surgeon to be most conservative concerning the prognosis.

HAROLD F. FALLS

MATERNAL VIRUS INFECTIONS AND INFANTILE MALFORMATIONS

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Ann. d'Oculist., 1956, *189:* 269–302

Gregg (Tr. Ophth. Soc. Australia, 1941, *3:* 35) was the first to observe the relationship between maternal rubella and congenital cataract, and other systemic malformations. The malformations caused by maternal rubella may be difficult to distinguish from genetic disturbances, and recognition of their origin depends on the presence of various associated defects of the eye, ear, and heart.

Congenital cataract is the abnormality most commonly observed. It is usually bilateral but may be unilateral; it is generally incomplete and when so, is always central, and the lens in which it occurs is frequently very small. Microphthalmy is often found in association with cataract. Three types of retinal dystrophy have been described: (1) gross migration of pigment throughout the eye; (2) small areas of peripheral pigmentation; and (3) a lacunar picture associated with a waxy optic atrophy. Other ocular malformations which have been reported include congenital glaucoma, corneal opacities, corneal edema, iris atrophy, anisocoria, coloboma of the iris, mesodermal dysgenesis, persistent pupillary membrane, heterochromia iridis, and hypoplasia of the ciliary body. Anomalies of the lens other than cataract include subluxation, lenticonus, and pigmentation of the posterior lens. Retinal abiotrophy of the Sorsby type, optic atrophy, retinal vein thrombosis, dacryostenosis, ptosis, and strabismus and nystagmus have also been reported with varying degrees of frequency.

Deafness and disturbances of balance are found in many patients; in fact, the proportion of congenital deafness attributable to rubella has been set as high as 64 per cent by Meyer and 72 per cent by Martin. Visceral lesions are common, with congenital heart defects occurring in about half the cases. A certain degree of brachymicrocephaly, which appears to be characteristic of the condition, has been reported in 11 per cent and 15 per cent of cases in two series. Mental re-

tardation is a common evidence of central nervous system involvement, and anomalies in other systems have been found by various authors in scattered cases.

Clinical signs other than malformations include a typical appearance, with fine, blond hair, skin with little pigmentation, oblique palpebral fissures, and very delicate cartilage in the nose and ears. True mongolism has also been attributed to maternal rubella by Gregg and others. Prematurity is a frequent finding (34.5 per cent in one series); the infants are often hard to feed, and many show psychomotor retardation.

The differential diagnosis can be made more easily if it is remembered that, apart from the clinical signs referred to, embryopathy resulting from rubella is always characterized by the presence of malformations: very few cases can be found in which one of the three principal localizations is absent. The two typical associations on which a diagnosis can be based are (1) the coexistence of ocular anomalies (cataract) and congenital cardiopathy, and (2) the coexistence of deafness and congenital cardiopathy. Heart defects are associated with cataract as often as with deafness; the association of deafness with ocular defects, however, is exceptional and depends on the date of the maternal infection. The earlier the date of the mother's illness, the greater the probability that the lens will be affected, because it develops more rapidly than the inner ear (two months for the lens as against three months for the inner ear).

If the mother contracts rubella during the first three months of pregnancy, the fetus may either die prematurely (abortion), or at birth (stillbirth), or show evidence of embryopathy. The number of infants affected varies from 10 to 50 per cent, according to epidemic conditions and the virulence of the rubella virus. Maternal infection with other viruses, especially those of mumps, varicella, poliomyelitis, and infectious hepatitis, may also be responsible for the development of embryopathy.

Prophylaxis and treatment may be applied to the mother during and before pregnancy, and to the infant after birth. Given the benign character of rubella itself and the severity of its effect on the fetus, active preventive immunization before pregnancy, preferably, in fact, before marriage or puberty, is strongly to be advised. Failing this, pregnant women in danger from exposure to rubella should be isolated and treated with passive immunization by convalescent serum or gamma globulin during the period of incubation (about two weeks). The number of cases in which the child is normal despite maternal infection makes prophylactic abortion ethically unacceptable, although some authors have advocated it in certain instances. Children with congenital defects due to rubella should be treated by prompt operative removal of cataract when it is present, so that the development of their vision and intelligence may be facilitated. Deafness is incurable in these patients, but mutism resulting therefrom can and should be overcome. Associated heart defects sometimes respond to surgical treatment, and other anomalies, such as harelip and hypospadias, should be corrected whenever possible.

Comment: François and Verriest have presented a thorough and well written review of this subject. Gregg's point that cataract of rubella origin is very frequently accompanied

by other systemic malformations, particularly of the heart, brain, and ear, is given careful emphasis. This knowledge is indeed valuable in any differential diagnosis when the ophthalmologist is confronted with sporadic cases of congenital ocular pathology.

The touchy subject of prophylactic abortion, when the pregnant female has been exposed to rubella or other viral diseases, is mentioned only to be discredited, and rightfully so, in light of present available statistics and knowledge.

Again, we wish to emphasize that no ophthalmic history is complete unless one has meticulously inquired concerning the course of the concerned pregnancy.

HAROLD F. FALLS

OXYGEN AND PREMATURE INFANTS

The accumulated evidence definitely incriminates the excessive use of oxygen as a major factor in the cause of retrolental fibroplasia in premature infants. "Excessive use" implies concentration of more than 40 per cent or the prolongation of administration after the indication for its use has passed. It is possible that even after periods of administration of higher concentration may be harmful.

On the other hand, the intelligent use of oxygen can be the means of saving the lives of hypoxic, dyspneic, and cyanotic babies. It would be unwise to arbitrarily deny adequate oxygen (and perhaps life) to those babies because of possible injury to the eyes of some.

Accordingly, the following recommendations are made: (1) Oxygen should be prescribed only on medical order the same as any drug or treatment (except in emergency). (2) Oxygen should not be administered routinely but only upon specific medical indication. (3) Oxygen concentration should be kept at the lowest possible level that will relieve the symptoms for which it is given, if possible not over 40 per cent. (4) Oxygen therapy should be discontinued as soon as the indication for it has passed. (5) Ordinarily, the indications for supplemental oxygen are general cyanosis (not acrocyanosis) and dyspnea. The urgency of treating these symptoms must rest with the clinical judgment of the attending physician. (6) Oxygen concentration must be determined by means of an oxygen analyzer as often as necessary to keep it properly stabilized, but at least every four hours. (7) A source which does not contain or deliver more than 40 per cent oxygen will insure against exceeding that concentration but may not be adequate in those occasional instances where higher concentration is desired. If such a restricted source of oxygen is employed, additional oxygen should be available for those special instances where it is indicated. (8) There are no apparent contraindications to the use of supplemental oxygen in infants weighing more than five pounds.

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Prepared by the committee on the fetus and the newborn infant of the American Academy of Pediatrics, Evanston, Illinois. Correspondence, J. A. M. A., 1956, **161:** 1275.

SYSTEMIC DISEASE

ADRENALECTOMY FOR VASCULAR DISEASE OF DIABETES

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Lancet, 1956, *1:* 530–534

The most urgent clinical problem in diabetes is the vascular disease which seems to develop inevitably if the patient lives long enough. Those whose diabetes starts after the age of 50 may live to old age without apparent acceleration of arterial degeneration, but the young are condemned to certain death from a characteristic disorder of small vessels, if the other hazards of diabetes are avoided. Now that these other hazards are becoming relatively unimportant, the patient with advancing vascular disease is rapidly becoming more common. That vascular disease, both atherosclerosis and capillary damage, is more common in patients with diabetes than in nondiabetic subjects is the finding of all substantial inquiries both in living subjects and in those who have died. Capillary lesions are seen with increasing frequency the longer diabetes persists, but atherosclerosis, though more than usually common, seems not to be related to the duration of the disease.

Atherosclerosis and diabetic "angiopathy," as Lundbaek called the capillary disease of diabetes, may be considered separately; it is not to be assumed too readily, however, that they are unrelated, for it must be remembered that the angiopathy can be detected in the retina at a very early stage and in the kidney by inference from examination of the urine, whereas atherosclerosis can only be diagnosed in life by rather gross clinical signs. At present there is no conclusive evidence that the arterial lesions differ from those of patients without diabetes. The capillary lesions, on the other hand, present a picture that is becoming more clearly defined as that of diabetic angiopathy.

The histological changes in the retina described by Ballantyne and Loewenstein (1943) remain specific for diabetes. Similar, though not identical, changes have been found in nondiabetic eyes, but the over-all picture is entirely individual. The same is true of the renal disorder, and the relation of the nodular lesions in the glomeruli to diabetes has been generally accepted. Apart from othe resemblances, the staining reactions of the hyaline material with the periodic-acid stain suggest that the lesions in the kidney and the retina are manifestations of a single disorder. Studies of necropsy material have demonstrated their coexistence in all fatal cases. This angiopathy, which is believed to be a specific complication of diabetes, is now under consideration for possible relief by adrenalectomy. Though the lesions may arise elsewhere than in the kidney and the retina, it is in these sites that the symptoms which justify a desperate remedy occur.

The establishment of a firm criterion for such an operation requires consideration of the clinical course of the retinopathy and the nephropathy in the absence of specific treatment. The stages in the evolution of diabetic retinopathy were classified by Ballantyne as follows: (1) changes chiefly in the central area; microaneurysms with or without punctate hemorrhages and punctate exudates; (2) dot and blot hemorrhages; confluent waxy exudates; (3) changes in the veins; increasing hemorrhages in the retina and vitreous; massive exudates; retinitis proliferans; and detachment of the retina; and (4) further increase in the vascular changes, with increased vitreous hemorrhages and exudates, and destruction of the retina.

Little has been written about the duration of these stages and their prognosis, but it has been shown that they do not necessarily occur in succession. Stage 1, for example, may pass directly to stage 3. It seems certain, however, that diabetic retinopathy will develop in every diabetic patient who lives long enough, and that the final stage of blindness will arrive in those who do not first succumb to renal failure.

The earliest lesions of glomerulosclerosis are almost certainly present for months or years before albuminuria, its first clinical manifestation, becomes apparent. Like the early changes in the retina, they may remain symptomless for prolonged periods. From the prognostic point of view, it seems clear that the appearance of albuminuria in a patient with long-standing diabetes, unless it can be attributed to active urinary infection or to gross cardiac insufficiency, indicates the onset of glomerulosclerosis. Hypertension, impaired renal function, and perhaps edema eventually appear and death from renal failure or congestive heart failure usually occurs in from two to five years.

Acceptance of the premises that the vascular disease of diabetes is progressive and that it leads ultimately to disablement and death, and that adrenalectomy deserves consideration as a possible means of arresting this progress, brings one to the difficult problem of selecting the cases in which it may legitimately be used. The earliest detectable lesions in the retina may remain stationary for years, and only an extreme enthusiast would consider so drastic an operation as adrenalectomy at this stage. On the other hand, the later stage of retinitis proliferans or of renal insufficiency is almost certainly beyond the possibility of reversal by any form of treatment. The period during which the operation seems warranted, therefore, is one in which it can be said that the vascular disease has reached a point from which it will, if untreated, inevitably progress to blindness or renal failure within five years, though it has not yet caused irreversible damage. Such a period may be brief and those in whom vascular disease has been detected must therefore be examined frequently.

The positive indications for adrenalectomy seem to be (1) retinitis proliferans as soon as diagnosed; and (2) glomerulosclerosis of a degree characterized by the following positive features: albuminuria constantly present for six months; a diastolic blood pressure above 90 mm. Hg after a week of rest in bed; and diabetic retinopathy. The operation, on the other hand, is contraindicated in patients with advanced renal disease, as shown by a blood-urea level persistently above 70 mg. per 100 ml. in the absence of fluid and electrolyte disturbance from vomit-

ing or uncontrolled diabetes, because in such patients adrenalectomy is apt to aggravate renal failure. The progressive deterioration found in most patients with diabetic retinopathy makes early operation advisable. An occasional patient may, it is true, be operated on unnecessarily, but since the procedure is safe and the postoperative maintenance need not be burdensome, the risk of such unnecessary operations must sometimes be taken if a good functional result is to be obtained.

Follow-up of from 5 to 16 months of 6 diabetic patients ranging in age from 31 to 60 years in whom total adrenalectomy was tried for the relief of severe vascular disease showed the following results: retinopathy was improved in 1, unchanged in 3, and worse in 1; the sixth patient, who was already uremic when operated on, died from renal failure two weeks later. Albuminuria was unchanged in the 2 patients in whom it was found before the operation. Control of the diabetes was unchanged. The general health was better in 1 patient and unchanged in the others.

Comment: During the past five years increasing evidence has been accumulated to incriminate the adrenal cortex in the pathogenesis of the nephropathy and retinopathy complicating diabetes. This may be an excessive production of glucocorticoids, the production of abnormal steroids, or factors concerned with the utilization of oxysteroids in long-standing diabetes. It has been emphasized repeatedly, however, that the hypothesis is based upon tenuous observations and remains neither proved nor disproved to date.

Based upon this hypothesis, several investigators have attempted to decrease adrenocortical activity clinically. This has been accomplished by hypophysectomy (Luft and Olivecrona, 20 cases; Kinsell, 5 cases) or bilateral adrenalectomy (Green, 1 case; Wortham and Headstream, 7 cases; Malins, 6 cases). All observers report encouraging results. However, the cases selected in almost all instances have had far advanced retinopathy with proliferative changes. In such eyes, one can draw no objective conclusions as to the effects of therapy upon the basic disease process. This is particularly unfortunate for these glandular extirpations are disabling procedures (especially hypophysectomy). On the other hand, it is entirely understandable that only those diabetics with advanced visual loss volunteer for such experimental damaging surgery. The fact that these procedures can be accomplished successfully and patients maintained reasonably on replacement therapy has been a most important contribution. It now remains to evaluate objectively whether or not the capillary lesion characterizing diabetic retinopathy can be prevented.

Additional notes of caution which should be re-emphasized are the extremely variable course of early diabetic retinopathy and the necessity for long-term (2-3 years) ophthalmoscopic follow-ups in large series before too hasty conclusions are drawn.

BERNARD BECKER

KERATOCONJUNCTIVITIS SICCA AND RHEUMATOID ARTHRITIS

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Ann. Rheumat. Dis., 1956, *15:* 21–25

Far from being a rarity, keratoconjunctivitis sicca is in reality the commonest ocular complication of rheumatoid arthritis. Evidence of lesions of the sicca type was found in 30 (14.3 per cent) of 210 former in-patients of the Rheumatic Diseases Unit, Northern General Hospital, Edinburgh, while only 7 patients (3.3 per cent) showed signs of active or old uveitis. These findings agree substantially with those of other workers. Lesions of the lacrimal secretory nerves or of the gland parenchyma may be responsible in a few rare cases for the deficient lacrimation and resulting corneal and conjunctival lesions of keratoconjunctivitis, but in most cases no local ophthalmic cause for their development can be found. Although the term Sjögren's syndrome is generally applied to any condition in which the classical triad of keratoconjunctivitis sicca, polyarthritis, and salivary gland enlargement, first described by him, is present, opinions differ as to the significance of the arthritis. Some authorities consider it to be an incidental finding, while others believe that keratoconjunctivities sicca and its associated pathological states should be regarded as a part of rheumatic disease in its wider concept.

Rheumatoid arthritis was present in 14 (77.7 per cent) of 18 patients with severe or moderate keratoconjunctivitis sicca treated by the authors in the last three years; milder signs and symptoms consistent with a condition of conjunctivitis sicca were also found in 16 others with rheumatoid arthritis. This high percentage of cases associated with polyarthritis was due to the fact that most of them were identified at a rheumatic unit. The sex ratio of the 210 patients studied was 2.7 female to 1 male, but that of the 30 patients with keratoconjunctivitis sicca was 6.5 female to 1 male, 26 being women. Several ophthalmic features of interest were noted in the present series. The ocular symptoms ran a course of remissions and exacerbations, but symptoms were rarely completely absent in the severe cases. The waxing and waning of the ophthalmic symptoms in patients who also had rheumatoid arthritis often occurred independently of any changes in the arthritic condition. Furthermore, the severity of the ocular changes in such patients was not proportional to the severity of the arthritis, some of the most marked examples of keratoconjunctivitis sicca being encountered in patients with mild or quiescent rheumatoid arthritis.

Although ocular discomfort, photophobia, and mild impairment of vision are well recognized as symptoms of keratoconjunctivitis sicca, the more serious risk to vision associated with this condition have not been fully appreciated. In the present series, corneal ulceration was noted in 3 cases. In 2, the ulcers

were of the small marginal type and healed without incident. In the third, however, the corneal ulceration was bilateral, and the patient was initially referred to the hospital when perforation of a central corneal ulceration necessitated enucleation of the eye. One patient also had a small pannus involving the inferolateral quadrant of the cornea.

The histologic changes in the lacrimal glands consisted of round-cell infiltrations, atrophy and destruction of the acini, and replacement fibrosis in the later stages. The lesions in the lacrimal glands were considered to be mainly responsible for the dryness of the eyes and the subsequent epithelial changes. Primary degenerative changes in the conjunctival epithelium could also contribute to the appearance presented by developed keratoconjunctivitis sicca. The changes noted in the lacrimal glands are similar to those found in the salivary glands but one important difference is that while secretory ducts may be blocked in the salivary glands, blocking of the lacrimal glands does not occur. This is in keeping with the clinical observation that enlargement of the salivary glands is not uncommon in Sjögren's syndrome, but that enlargement of the lacrimal glands is never seen.

Various conditions have been recorded as being associated with this disease, but as a rule only two, polyarthritis and xerostoma, are present. Many of the associated conditions can be attributed to a deficiency of epithelial glandular secretions and the consequent dryness of cutaneous and mucosal surfaces. Trophic nail changes were apparent in 4 of these patients and 3 had external otitis of a kind that might be described as otitis externa sicca.

General treatment has proved valueless, and no local treatment intended to relieve the ocular symptoms has yet been entirely successful in increasing lacrimal secretion. Artificial tears, which do not evaporate so rapidly as saline and antibiotic eye drops, are beneficial in many mild cases. Systemic administration of the steroid hormones may relieve the ocular symptoms in severe and chronic cases, even though the lacrimal secretion is not increased. Topical administration of cortisone and hydrocortisone has proved to be a safe and useful method of treating mild and moderate cases. Local application of these hormones has been shown to be effective solely by virtue of their anti-inflammatory action, as no increase in lacrimal secretion has been noted during their use. Operative sealing of both lacrimal puncta in order to conserve diminished secretions is an effective surgical procedure but it should be used only in the more severe cases. The resulting increase in lacrimal secretion may be slight but the subjective and objective improvement in the eyes is sometimes appreciable.

Comment: Sjögren described a triad of clinical features characterizing the syndrome that bears his name. This included keratoconjunctivitis sicca, xerostoma, and polyarthritis. However, larger series of patients with keratoconjunctivitis sicca revealed many cases in which polyarthritis was absent, and the question has been raised as to whether arthritis is a part of the syndrome.

The present authors review a series of 18 patients with keratoconjunctivitis sicca and report arthritis in 14 of them. Furthermore, the arthritis was considered to be rheumatoid in all instances. However, their cases were referred from a "rheumatic unit" which probably accounts for the high incidence of rheumatoid arthritis in this series.

On the other hand, the authors confirm the findings of Holm of a startlingly high (13 per cent) incidence of keratoconjunctivitis sicca in a series of rheumatoid arthritis patients. Although emphasis in the past has been placed upon such ocular involvements as non-granulomatous uveitis, episcleritis, and scleromalacia perforans, in the present series keratoconjunctivitis sicca was "the commonest ocular complication of rheumatoid arthritis." Thus, in their series of 210 patients with rheumatoid arthritis, keratoconjunctivitis sicca occurred in 30 (14.3 per cent) and uveitis in only 7 (3.3 per cent).

However, it is important to appreciate that no relation was noted between severity of arthritis and the sicca syndrome, nor did the two tend to correlate in time. Furthermore, the production of tears in keratoconjunctivitis sicca does not appear to increase following administration of corticosteroids or salicylates. Symptomatic treatment, such as artificial tears, remains the therapy of choice. It is clear that much more basic information is needed about the disordered physiology of this interesting disease process.

It may be of interest to the reader to record 1 female patient, aged 55, with bilateral Fuchs' endothelial dystrophy, corneal edema, and marked visual impairment (below 20/200). The poor prognosis had been explained to this intelligent patient. She returned three years later with keratoconjunctivitis sicca and less than 1 mm. of tears by Schirmer's test. Although she now complained of scratchiness, irritation, and dryness of her eyes (as well as her mouth), the corneal edema had cleared sufficiently to permit 20/40 to 20/50 vision in spite of evident endothelial damage. Improvement in visual status has persisted under observation for the past 18 months.

BERNARD BECKER

AN APPRECIATION OF WASSERMANN IN RELATION TO OCULAR SYPHILIS

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A.M.A. Arch. Dermat. & Syph., 1956, *73:* 464–468

Primary optic nerve atrophy of acquired syphilis is the outstanding cause of blindness in relation to syphilis. Experience in the clinic for ocular syphilis at Wills Eye Hospital suggests that 90 per cent of blindness and industrial blindness caused by syphilis can be attributed to optic nerve atrophy of acquired and of congenital syphilis. Next in order of frequency come interstitial keratitis, iritis (acquired syphilis), optic nerve atrophy secondary to optic neuritis, and retinochoroiditis of congenital syphilis. The less frequent and rare causes are gumma of periostitis of the orbit, choroiditis (acquired syphilis), severe intraocular inflammatory processes of acquired syphilis, and gumma of the various components of the eye, including keratitis pustuliformis profunda. In congenital syphilis, the choroid and the cornea are most susceptible to involvement by the disease, the frequency of involvement being comparable to that of the osseous system. In acquired syphilis, on the other hand, the iris is more susceptible, the choroid is considerably less so, and the cornea is only rarely affected.

The decline in the incidence of syphilitic infection and of congenital syphilis in the continental United States has been accompanied by a corresponding decline in the various forms of ocular syphilis. Syphilitic uveitis (iritis, cyclitis, iridocyclitis), which was seen to decline in 1944, subsequently disappeared completely. Its disappearance accompanied that of early syphilis, not a single case of the disease in its primary or secondary form having been seen at the Wills Clinic since about 1945. So far as blindness and industrial blindness are concerned, syphilitic uveitis is less important than interstitial keratitis and optic nerve atrophy. Studies of the final visual acuity in 61 eyes in a series of 72 patients with syphilitic uveitis reported on by the author in 1946 showed that 4 patients were industrially blind in one eye; 1 patient had no visual acuity in one eye; and 1 was industrially blind in both eyes. In 12 of the 72 patients, the disease was of the iridorecidivous type, that is, iritis occurring after inadequate treatment of early syphilis. In its biologic significance, this corresponds to neurorecurrence (neurorecidivism). Iridorecidivism was not observed in any of 17 patients with syphilitic uveitis who were treated with penicillin, first used in 1944, although 1 had a cutaneous relapse 10 months after treatment. Penicillin therapy will probably eliminate iridorecidivism, because it is more apt to be adequate than arsenical and bismuth therapy and patients are less likely to abandon the treatment before it is complete.

Perhaps the second most frequent ocular involvement of secondary syphilis is optic neuritis. Next come the relatively rare severe intraocular inflammatory processes, including disseminated chorioretinitis, often called the Förster type. Patients with these ocular lesions of early syphilis are no longer seen at the Wills Clinic, and this again is in harmony with the decline in the incidence of early syphilis.

A gradual and progressive decline in the number of patients with initial attacks of interstitial keratitis of congenital syphilis began to appear in 1946, seven years after Pennsylvania's enactment of the premarital and prenatal examination laws requiring appropriate serologic tests for syphilis before marriage and during pregnancy. As a result of these measures and similar laws enacted in most other States, the birth of a syphilitic baby has become an anachronism and new cases of interstitial keratitis seldom occur. Patients now seen at the Clinic are chiefly those who have either a recurrence of old interstitial keratitis or initial involvement of the second eye; among the few who have an initial attack, most were born either out of wedlock or of parents married in states without premarital or prenatal laws. The decline in early congenital syphilis has also been paralleled by the complete disappearance of other ocular lesions associated with the disease in its early stage. Optic nerve atrophy of acquired syphilis was the last of the ocular lesions to show a decline. This condition is not apt to appear in patients in their early twenties because a period of about 10 years at least must elapse before it reaches the symptom level. Undoubtedly, the decline in the number of new cases of early syphilis that became apparent in 1940 explains the disappearance of optic nerve involvement in the earlier age range and the fact that most of the patients now seen are in the older age groups. The widespread use of peni-

cillin for various diseases has probably resulted in the incidental treatment of many patients with asymptomatic syphilis and the consequent prevention of optic nerve involvement.

This report of the victory that has been won in controlling the devastating effects of ocular syphilis may well be both the author's swan song and the obituary of the Ocular Syphilis Clinic at Wills Hospital, once crowded with patients with white optic disks and white canes, but now relatively deserted. In contributing to the elimination of the scourge of congenital syphilis by his serologic test, Wassermann has won the gratitude of those whose eyesight has been conserved to see the beautiful—the starlit sky, the red of the rose, and the golden shafts of the setting sun.

PHOTOCOAGULATION

G. Meyer-Schwickerath of the University Ophthalmic Clinic and Institute of Experimental Ophthalmology of Bonn, Germany (Ann. d'Oculist., 1956, *189:* 532–548) states that the production of retinal trauma by sun eclipse has suggested the use of light as a treatment for retinal disease. After several trials with the sun and artificial lights, the author built an apparatus which is able to produce photocoagulation of the fundus without opening the eyeball. It is a type of ophthalmoscope with direct observation, and special lamp. With a normal light, the fundus may be observed. The light is then sent into the eye with the greatest intensity possible. A coagulation occurs which can be recognized by the appearance of white spots. Clinical and histologic examinations have shown that after a photocoagulation an adhesive scar may develop in the choroid.

The cases reported describe 91 macular holes with peripheral tears of which there were 22 cases of localized detachment spontaneously reapplied by rest; 28 cases of prophylactic coagulations on peripheral and degenerative retinal lesions; 11 cases received a coagulation of the total periphery of the retina. In 14 cases the photocoagulation was performed as complementary operation after a simple diathermy; eleven cases of perforating wounds in order to prevent a secondary retinal detachment; 6 cases of periphlebitis of the retina; 10 cases of tumors, melanosarcomas, gliomas, and angiomatosis of the von Hippel-Lindau's types.

There is no possibility of establishing a parallelism between the photocoagulation and the diathermic operation because the cases in which the two methods were successful are nearly the same. The advantage of photocoagulation lies rather in its extreme simplicity, and in the fact that operation can be performed several times without any risks to the patient.

The apparatus after a small modification can be used to produce an artificial pupil in the iris.

OCULAR INJURIES

EYE INJURIES IN NUCLEAR WARFARE

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Military Medicine, 1956, *118:* 286–292

Eye injuries in nuclear warfare should be treated according to a specific plan based on the following considerations: (1) the kind of injuries that will be produced; (2) the number that will be produced; (3) the personnel available to care for them; and (4) the facilities and supplies at hand. The injuries will be either blast, long-wave radiation, or short-wave radiation, alone or in combination. Short-wave radiation injuries develop at various periods after exposure; consequently, they do not require emergency care at the time of the disaster. Injuries due to long-wave radiation are burn injuries and may be either intraocular or extraocular in type. The intraocular or chorioretinal burns caused by atomic flash may be very severe at near distances, especially if they occur in the macular area. It should be noted that the distances at which these burns may occur are much greater than those at which nuclear weapons may exert any other harmful direct effect. Fortunately, these intraocular lesions do not require immediate treatment. Extraocular eye burns, however, whether flash burns of the eyelid and eyeball or secondary burns caused by fires started by the explosion, present a different problem. In flash burns, a very high percentage of the energy is delivered in such a small fraction of a second that the eyeball may be burned before the blink reflex can close the lids (in roughly 0.1 second). In burns due to heat from flames, however, the eyeball is much less apt to be affected because the blink reflex is ordinarily quite capable of protecting it from injury. The treatment of burns of each of these types is well known, but the fact that large numbers will probably have to be cared for within a short period creates a serious problem, all the more so because data on which to base an estimate of its magnitude are not as yet available.

Traumatic eye injuries from blast effects and flying debris may be expected to affect some 10 per cent of all hospital casualties in addition to those with intraocular and extraocular burns.

Four types of care will be required in the treatment of eye casualties: (1) initial care by the patient himself or by a member of the family or a roving first-aid team; (2) initial professional care, which will probably be given at a collection and screening station by a physician other than an ophthalmologist; (3) initial care by an ophthalmologist, given when the patients are being examined to determine the definitive treatment required for each; and (4) definitive ophthalmo-

logic care, which will ordinarily be given in a hospital. Certain injuries can be treated later without unduly increasing the risk to the patient's vision, but others must be cared for promptly if vision is to be preserved and enucleation of the eye avoided. Patients should be given definitive treatment in the following order according to the nature of their injuries: (1) those with perforating injuries of the globe; (2) those with severe burns affecting the globe; (3) those with severe lid lacerations; and (4) those with intraocular foreign bodies and contusions of the eyeball with or without intraocular hemorrhage and those with eye injuries of any other kind requiring opthalmologic care.

In order to carry out a plan of this kind, provision must be made for the training of personnel, the acquisition of supplies and equipment and their storage in suitable places, and the creation of a well-knit organization capable of putting it into effect.

Comment: Colonel Byrnes' plan for the management of eye injuries in nuclear warfare deserves careful attention not only from ophthalmologists but also from all concerned with civil defense. He faces the situation with entire realism. Should disaster strike, ophthalmic care will not be immediately available, and eye injuries, because they are not lethal, will not receive priority of medical care. Initial care, as Colonel Byrnes states, will not be professional, and initial professional care will not be administered by an ophthalmologist. The solution of the problem is therefore the training of personnel, the provision of supplies and equipment, and the creation of a functioning organization prepared to cope with disaster *before disaster strikes.*

GEORGE M. HAIK

Basic Sciences

BIOCHEMISTRY

DIABETIC CATARACTS: A REVIEW OF EXPERIMENTAL STUDIES

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Diabetes, 1956, *5:* 93–97

Efforts to prevent the complications that follow prolonged diabetes are hampered by ignorance of their cause. Not only may the diabetes itself be the result of a variety of metabolic defects, but the length of time usually required for the development of the complications may also make the acquisition of knowledge a slow and tedious task. It is therefore not surprising to find two opposing points of view concerning the relationship between the control of diabetes with insulin and the development of complications. Some believe that complications can be prevented by good control; others believe that complications develop in spite of good control.

Studies with animals may provide clues to the mechanism by which the diabetic complications are produced. Diabetes, when experimentally induced in animals, leads to the development of many of the complications associated with human diabetes, including cataract formation. Diabetic cataracts in rats develop through certain stages. At first vacuoles are observed around the periphery of the lens. Later, fine crystalline opacities develop centrally, and still later the lens suddenly becomes opaque. The last of these changes occurs over a period of from 24 to 48 hours and is readily seen with the unaided eye. This can be used as an excellent indicator of a metabolic end point. By relating various experimental conditions to the appearance of this end point, it is possible to gain an insight into the factors that may cause this complication of diabetes. In appraising the work that has been done in this connection, three points may be considered: (1) the relation of the severity of diabetes to cataracts; (2) diabetic factors that influence cataracts; and (3) evidence for a theory explaining the development of cataracts.

(1) Rats with experimentally induced diabetes have hyperglycemia, glycosuria, polyuria, polydipsia, and polyphagia. In spite of this last, however, they fail to gain weight at a normal rate. Any one of these findings might be used as an index of the severity of the diabetes, but the one that most closely represents the environment of the lens is the blood sugar level. Furthermore, the other changes are secondary, as shown by the fact that they can be reproduced by increasing the blood sugar level with another sugar such as galactose. The nonfasting blood sugar is readily measured. Although the hyperglycemia varies slightly from week to week, the average of several determinations on a single rat or group of

rats remains constant and serves as a useful measure of the environment of the lens. The time required for diabetic cataract formation bears an inverse relationship to hyperglycemia. Thus, a minimum time is required for the maturation of a cataract regardless of the height of the blood sugar, and a minimum elevation of blood sugar is required for the formation of cataracts. The minimal blood sugar is about 250 mg. per 100 cc. At this level, the renal tubular reabsorption mechanism for glucose is saturated with a resultant loss of sugar in the urine and a tendency to ketosis and neoglucogenesis. The relationship between the time required for the development of cataracts and the height of the blood sugar has led to the suggestion that the cataracts may be the result of one of the factors associated with diabetes, i.e., they may be caused by the "toxic" effects of hyperglycemia or acidosis, by the destruction of proteins in neoglucogenesis, by the loss of an essential metabolite in the urine, or by the failure to absorb glucose in the absence of insulin. The fact that cataract formation can be prevented by controlling these factors with insulin supports the belief that one or more of them may play a mediating role in the process by which cataracts are formed.

(2) The possible mediating role of the various factors present in diabetes may be studied by changing the relative severity of these factors in diabetic animals and noting the effect on the time required for cataract formation. Studies of this kind have shown that the administration of a high fat diet, fasting, and the administration of phlorizin, which increases the loss of sugar through the kidney and hence lowers the blood sugar, are beneficial in preventing cataracts. In each of these conditions, the blood sugar is lowered and the other metabolic changes of diabetes are aggravated. The general status as indicated by growth curves is not improved, and ketosis and neoglucogenesis are known to become worse. It seems, therefore, that hyperglycemia must play a direct role in the production of diabetic cataracts.

If the high blood sugar level acts directly on the lens to produce cataracts, then the amount of sugar reaching the eye by way of the blood stream should be of importance. This can be tested by altering the blood supply for one eye and using the second eye as a control. Thus, in galactose-fed rats cataracts are first seen in the left eye in 56 per cent of the animals. However, when one of the carotid arteries is ligated and cut, 90 per cent of the cataracts are first observed on the side with the better blood supply and hence the better supply of galactose. In diabetic rats, on the other hand, the occurrence of cataracts is not related to the blood supply. Since carotid ligation in normal rats does not cause cataracts and since carotid ligation in diabetic rats does not affect the side on which cataracts are first observed, it follows that cataracts in galactose-fed rats are related to the amount of blood and hence the amount of galactose reaching the eye. The failure of carotid ligation to influence cataract formation in diabetic rats thus leads one to question the hypothesis that hyperglycemia is directly responsible for the production of diabetic cataracts.

If diabetic cataracts are not the result of high levels of glucose working on the eye, then the role of hyperglycemia in producing cataracts must be reevaluated. Hyperglycemia has been implicated as a factor in cataract production because of the direct relationship between the height of the blood sugar and the rate at

which the cataracts appear and because their appearance can be prevented by lowering the blood sugar. Each of these points can be explained if it is assumed that cataract production is directly due to some factor that parallels hyperglycemia and that a lack of insulin is such a factor. If a lack of insulin produces cataracts, then cataracts are probably the result of an inability to obtain energy by utilizing glucose. Lowering the blood sugar with resulting ketosis would supply an alternate source of energy for the lens. If the total energy supply were thus raised above the critical level, cataracts would be prevented. Furthermore, if diabetic cataracts are the result of the inability of glucose, in the absence of insulin, to supply energy for the lens, the development of the cataracts would be independent of the blood supply. Thus the known facts can be explained by a mechanism that does not involve a direct action of hyperglycemia in the production of cataracts.

(3) The following mechanism is proposed for the development of diabetic cataracts. In the absence of insulin, the uptake of glucose by the lens is impaired. Since the lens depends on glucose for most of its energy, the total available energy is lowered beyond the critical point needed for the maintenance of transparency. The lens is also dependent on the constituents in the blood for alternate sources of energy. A decrease in available energy might produce cataracts by stopping the synthesis of various structural compounds or by blocking the maintenance of water and electrolyte balance. This hypothesis is supported by studies on glucose uptake in isolated lenses and on diets that supply energy-yielding substances other than glucose. The fact that a special fructose-high-fat diet providing energy-yielding substances which can be utilized in the absence of insulin prevents the development of cataracts, although the diabetic hyperglycemia is not lowered, definitely rules out hyperglycemia as a direct mediator in the production of cataracts. Furthermore, the use of this diet has a beneficial effect on many tissues of the body as shown by the growth curves of rats receiving it.

Comment: The most easily detectable metabolic defect in the diabetic is the elevation of sugar in the urine and blood. Since the aqueous is in a sense a filtrate of the blood, it was assumed that the elevated glucose level of the aqueous was in some way "toxic" to the lens and thus produced cataracts. With the rise of physical biochemistry this "toxicity" was interpreted as an alteration in the osmotic pressure relationships of the aqueous and lens. In a series of brilliant experiments of which this article is a summary, Patterson has shown that cataracts develop in the diabetic animal in the absence of a localized increase in glucose. What mechanism then can be postulated for their development? Largely through the work of Levine and his associates (Levine, R., Goldstein, M. S., Huddleston, B., and Klein, S. P.: Am. J. Physiol. 1950, *163:* 70; and Soskin, S., and Levine, R.: *Carbohydrate Metabolism*, Univ. Chicago Press, 1952) it has been shown that the point of action of insulin is at the cell membrane and in diabetes the insulin deficiency results in a breakdown of the transport of glucose into the cell. Patterson applies this hypothesis to the lens and feels that, in spite of the high level of glucose in the immediate environment of the lens, this glucose is unavailable to it and the result is an inability of the lens to meet its energy requirements. Since in a sense transparency is the "work" done by the lens a lack of "fuel" results in a lack of work and consequently a lack of transparency, i.e., cataract formation.

DAVID SHOCH

COLOR VISION

SPECIFICATIONS AND CALIBRATION OF THE 1953 EDITION OF THE INTER-SOCIETY COLOR COUNCIL COLOR APTITUDE TEST

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J. Optical Soc. America, 1956, *46:* 389–393

The current (1953) color aptitude test of the Inter-Society Color Council follows the pattern set by the 1944 edition, that is, it is a matching test employing duplicate saturation series of four colors with ten steps in each series. One set is mounted randomly by color on an easel; the other is held in a dispenser which presents one chip at a time (Fig. 1). Several improvements have been made in the format and structure of the test and in the durability of the materials, but none of these has made any change in its fundamental characteristics.

In the production of the series, pigment mixing was carefully controlled to meet colorimetric specifications. These were designated in Munsell terms, samples were measured with the spectrophotometer, and the C.I.E. coordinates of the series were calculated. The controls of production were so carefully maintained that there is no reason to believe that measurements of any other set will differ from the measurements of a given production set to a greater extent than a re-measurement of the same set by another operator using another instrument.

Very specific instructions were laid down both for the tester and for his subjects. Emphasis was placed on such conditions as intensity of illumination and angles of lighting and viewing. The order of presentation and the arrangement of the field chips were carefully planned to meet psychological and statistical requirements.

Because of the fineness of gradation in the series and in the light of experience with the preceding edition, it was considered necessary to score the test judgments not simply as "right" or "wrong." Therefore, although the highest weighting was given to the correct matches, matches made to neighboring chips in the series were accepted and given partial credit. In arriving at such score weightings, use was made of an item analysis of 200 tests which were obtained using the first sets produced for general distribution, before any were released.

A "predictive index" was derived by calculating, first, the average number of correct matches in each color series made by the entire group of 200 subjects, and secondly, by determining the average number of correct matches made by every group which made each particular judgment of match in a color series. In every case, it was found that the group of subjects who made a particular

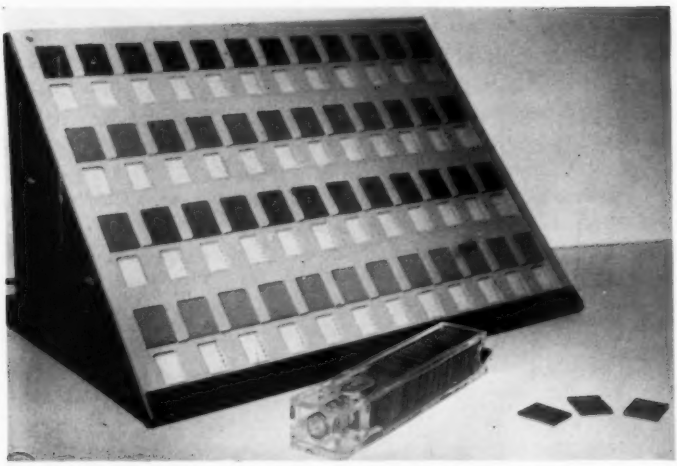

FIGURE 1. The Inter-Society Color Council Aptitude Test showing the easel in working position and the loose chip dispenser (Courtesy of Dimmick, F. L.: J. Optical Soc. America, 1956, *46:* 389–393)

match correctly had the highest average of additional matches correct in this color. Consequently, they were always above the average, 3.31, for the whole group. In order to make the results comparable from one color to another, the ratio of the correct matches for every group to the average for all subjects was calculated. The ratios so obtained are called "indices of prediction" because they indicate how much any match predicts about correctness of match in the rest of the test. Scores of 3, 2, and 1 were based on these ratios. That is, matches having ratios above 1.2 received a score of 3; those above 0.9 received a score of 2; those above 0.6 received a score of 1; and those below 0.6 received no score.

After the test had been in use in industries and laboratories, somewhat more than 700 score sheets were collected so that the score weighting and the norms could be re-examined on a more adequate basis. Since a test such as this is of interest primarily to industries and laboratories concerned with color control, these data may be assumed to have been obtained mainly from subjects who were either directly or indirectly concerned with color problems. The results were subjected to an analysis similar to the one made in the original standardization tests, and the indices of prediction were found to be substantially the same as they were for the standardizing group. No general alteration of the weighting system is indicated.

A distribution of 698 individual scores obtained by the system of weighting described was compared with a calculated normal distribution plotted on the same scale. In view of the somewhat selected character of the group, both the agreement and the divergence of the empirical with the calculated curve are of interest. Apparently the selective factors have not exerted much influence on

this population, since they have left the distribution substantially normal. On the other hand, the mode of the empirical curve is definitely above the mean and there are fewer scores just below the mean than would be expected in an unselected group.

The chief interest in a test of this sort, however, is in individual rather than group scores. Repeat tests were therefore obtained from 200 subjects so that the reliability of the test could be determined. Correlation between test and retest scores was found to be 0.55, which is significant to better than the 1 per cent level. The intrinsic reliability of the test is indicated by the increased correlation estimated by the Spearman-Brown formula if the test were increased in length. By retesting and combining the results so that the scores represent 80 matches, r becomes 0.71. With four testings (160 matches), it would be raised to 0.83. In this way a final score of high precision can be obtained. A study of changes of score from the first testing to the next showed that there is no expectation that a man will do better or worse the second time than he did the first. The sum of all the improvements in score is equal to the sum of all the losses in score. Analysis of the changes in score shows that small changes of from 0 to 6 points predominate. The median change is less than 6 score points, which are equivalent to two of the 40 matches.

A few subjects made fairly large changes in score, which must reflect either instability in their performance or poor control of test conditions. Such instability in the performance of a subject, if it persisted, would signify unreliable color matching.

Comment: Any ophthalmologist or optometrist who is consulted by local industries is likely to be asked to help evaluate the "color aptitude" of existing or prospective personnel. It is important to understand what is involved in this matter, and how much it differs from a determination of normal color vision versus color blindness. The color blind is unable to see any difference between color stimuli which differ considerably, or even very greatly, for the normal. Color aptitude is the ability to see a color difference between color stimuli which differ only slightly. This ability may be good, bad, or indifferent in either a color-normal or a color-blind person. A color-blind man may match a bright red to a rich green, but if he is shown two shades of red (or two shades of green) he may see a difference between them as readily as many a normal (i.e. non-color-blind) man.

Industries whose products are colored do not want to employ color-blinds, or normals either if they have medium or low color aptitude. The former are readily screened out by accepted tests for color blindness, but such tests do not evaluate color aptitude. Tests which purport to do so are few and far between, and the only one that even has the words "color aptitude" in its name is the one evaluated in this paper. The paper does not reveal that the test takes a long time to administer, exasperates the testee, and actually measures only one of two functions that enter into color aptitude but are quite independent—the same subjects showing different rank orders for each, at different points along the spectrum.

These two functions are the ability to detect a tiny difference of dominant wavelength where there is no difference of saturation, and the ability to detect a tiny difference of the purity where there is no difference of hue. In the first performance the testee looks

for a difference of hue at constant saturation; in the second, he looks for a difference of saturation at constant hue. The ISCC test asks of him only the second of these performances. The first of them (and only this one) is demanded by the Farnsworth-Munsell 100-Hue Test—which, also, is very time-consuming, hard to take, and hard to score.

All this is by way of warning to the practitioner, against being as ready to agree to measure color aptitude as he is to screen for color blindness. It is a job for experts who are not to be found in the medical sciences, but in the field of colorimetry. It is a good thing for the ophthalmologist or optometrist to know what color aptitude means, but if he is asked to "measure" it, he is well advised to pass the buck to the nearest colorimetrist.

GORDON L. WALLS

OVERTREATMENT

Pill boxes are in vogue again, and some patients like to point out their various medicines and recite what each will do. Prescribing has reached the place where the side-effects from one drug are to be offset by using another, and, perhaps, it will soon be popular to administer a third to do away with the bad effects of the first two. It appears today to be unpopular to believe that the human body has any defensive or healing attributes. A few remarkable so-called "wonder drugs" have fostered a tolerance and acceptance of many unremarkable ones. Overtreatment is the use of too much medicine for any disease or its symptoms, and its extent is reflected by the difficulty in finding the etiology in drug eruptions. Often so many remedies are mixed in the system that it takes weeks of eliminative study to detect the guilty one. Finding the drug inducing a blood dyscrasia is sometimes impossible because so many were taken. . . . Some risk is permissible in those diseases with a serious prognosis, but drug toxicity in self-limited disorders is another matter. (L. E. Gaul, M.D., Overtreatment Dermatitis, *Annals of Allergy*, November–December, 1955.)

OPTICS

EFFECT OF STIMULUS DURATION ON ELECTRICAL RESPONSE OF THE HUMAN RETINA

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Psychophysical data show that, in determining whether or not a flash of light will be seen by the dark-adapted eye, the two stimulus variables of duration and intensity are in reciprocal relationship, which holds for exposure times below a certain *critical duration*. Above this value, increases in the duration of the flash become progressively less effective until ultimately seeing is dependent on intensity alone. When the visual stimulus is restricted to small peripheral areas the changeover from the one relationship to the other occurs abruptly at a flash-duration of a little more than 100 msec.

A similar critical duration characterizes the electroretinogram in invertebrate and lower vertebrate eyes. The present study was made to determine whether stimulus intensity and duration are similarly related with respect to their effect on the human *b*-wave. The electrical responses occur at levels of stimulus intensity which are considerably above the visual threshold.

The size and form of the *b*-wave of the human electroretinogram was dependent on the duration as well as on the intensity of the stimulating light. In determining the amplitude of submaximal *b*-waves, intensity and duration shared equally until a certain critical duration was reached. Above this critical duration of about 100 msec. in the dark-adapted eye, less under conditions of light adaptation, amplitude was determined by intensity alone. The latency of the response, however, was determined without reference to the stimulus duration. It is interesting to note that a critical duration of just over 100 msec. has also been reported from psychophysical studies of the dark-adapted eye in which visual threshold rather than electrical response criteria were used.

Comment: This well organized short paper reveals a number of interesting data. We find another confirmation of the fact that a dark-adapted eye, while giving larger responses, is slower in responding. We see again that both intensity and duration of a light flash affect the magnitude of response and that latency (e.g., the time from onset of light flash to initial rise of *b*-wave) decreases with increasing stimulus intensity being at the same time independent of the latter's duration. We learn furthermore that increasing duration of stimulus prolongs the response. (This is less noticeable when stimulus intensity is large.) The amplitude of the *b*-wave increases with increasing duration up to a critical time limit, but it is independent of duration in case the intensity of stimulation is so great as to produce maximal deflection even at 10 msec., the shortest stimulus durations available with the authors' experimental setup. The critical duration was found to be

about 30 msec. in partial light adaptation and 100 msec. in dark adaptation, provided that the stimulus intensity was below about 10 ft—Lambert. Analytical treatment of the data shows that when the stimulus is energetic enough to elicit a response but of insufficient duration to produce a maximal response, the magnitude of the response is roughly a linear logarithmic function of the energy of the stimulus [the product $I \times t$ (Intensity $\times$ time)]. Of course, the authors themselves realize that their suggested equations to correlate response with either I or t or the product of the two, have only "descriptive significance," since the linear relationship breaks down both at durations below the ones employed and at high intensities. In fact, the occurrence of a limiting magnitude of the *b*-wave in these experiments and the probability of the existence of a minimum value suggest that a sigmoid curve would better fit the actual values. Within limitations, however, $I \times t$ is constant for any selected amplitude of the *b*-wave and beyond the critical time limit, it is only I that counts. There is another point of interest stressed by the authors: Responses which are equal as far as the amplitude of the *b*-wave is concerned, are not necessarily identical in other respects, e.g., the latency periods or the times from onset of stimulus to peak of response might be quite different. As far as these latter values are concerned, the authors found them different in dark and light adaptation (they are shorter in light adaptation) and they become shorter with increasing intensities of stimulation, even if the experimental conditions are so modulated that the amplitude of the *b*-wave remains the same.

ARTHUR LINKSZ

THE DISCREPANCY BETWEEN PHYSICAL AND PERCEIVED CURVATURE

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Am. J. Optom. 1956, *33:* 148–154

(Because of the complexity of the original paper comments have been inserted in the condensation itself by the Section Editor, Dr. Arthur Linksz.)

This paper represents a significant contribution and ophthalmologists interested in problems of space perception should be able to appreciate at least some of the points made by the author. Since it is essentially a mathematical essay, it will be impossible to discuss its contents without referring to some of the formulas upon which the argument is based, though the derivation of these formulas will be mostly omitted. (It is hoped furthermore that even those will be able to follow the author's main line of thought who skip the formulas.)

Any point P in the physical space which contains the eyes and visible objects (this reviewer called this particular type physical space the "visible" space and feels disappointed that his terminology has not been adopted) is characterized by the equation,

$$\gamma = \frac{2a \cos \phi}{\rho} \qquad (1)$$

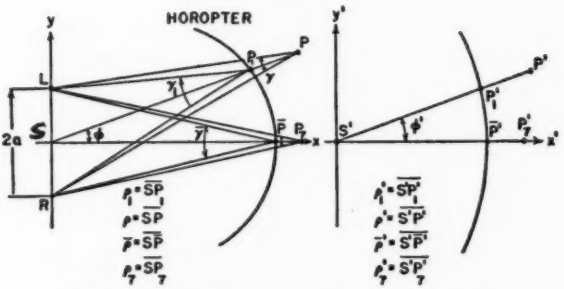

FIG. 1. Relationship between various points in physical space and their counterparts in visual space. The x-axis passes through the point of fixation $\bar{P}$ and the midpoint S of the interpupillary line connecting the pupillary centers R and L. The Y-axis is perpendicular to the x-axis at S. P is any point in the plane of regard on the radial vector SP at an angle ϕ from the x-axis and at a distance ρ from S. γ represents the binocular parallax of the point P. (Courtesy of FRY, G. A.: Am. J. Optom. 1956, *33:* 148–154).

where γ is the angle between the two lines of direction, $2a$ the distance between the eyes, ρ the distance of P from S (the midpoint between the eyes), and ϕ the angle formed between the sagittal or x-axis originating at S and the line $PS = \rho$. For very small angles ϕ the equation changes to

$$\gamma = \frac{2a}{\rho} \tag{2}$$

In visual space, there is a point P' which corresponds to P of visible space. This point is seen at a subjective inclination angle ϕ' relative to the straight forward direction, an angle which is assumed to be equal to ϕ.

If a point P happens to be on the x-axis ($\phi = 0$), it becomes in the author's nomenclature designated as P_γ and its spatial characteristics according to equation (2) change to γ_γ, and ρ_γ. If the point happens to be the point of symmetrical bifixation, then it is designated as $\bar{P}$ with the characteristics $\bar{\gamma}$ and $\bar{\rho}$. Assuming now that a point P_γ on the x-axis is farther from the observer than $\bar{P}$, then there will be an angular disparity $\bar{\gamma} - \gamma_\gamma$ between their projections upon the eyes and since the γ and ρ values are related by equation (2), the following relationships

$$\bar{\gamma} - \gamma_\gamma = \frac{2a}{\bar{\rho}} - \frac{2a}{\rho_\gamma} \tag{4}$$

and

$$\frac{1}{\bar{\rho}} - \frac{1}{\rho_\gamma} = \frac{\bar{\gamma} - \gamma_\gamma}{2a} \tag{4a}$$

will exist between the respective distance of $\bar{P}$ and P_γ from S and their angular projections $\bar{\gamma}$ and γ_γ upon the eyes.

Now since $\bar{P}$ is assumed to be bifixated, $\bar{\gamma}$ will be the angle formed by the re-

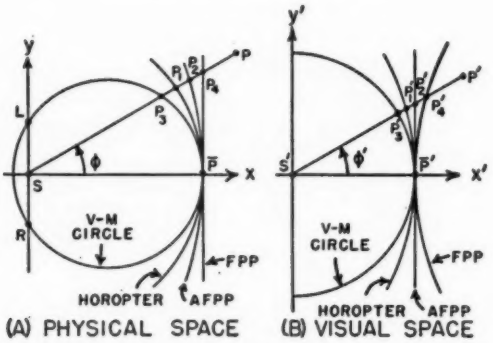

FIG. 2. The relationship between various curves in the X, Y plane of physical space and their counterparts in visual space. (Courtesy of FRY, G. A.: Am. J. Optom. 1956, *33:* 148–154)

spective lines of direction of two corresponding retinal points (the foveas), while γ_7 becomes the angular characteristic of retinal points which are disparate, the degree of their disparity obviously depending on the magnitude of $\bar{\gamma} - \gamma_7$. So far, of course, the author has been dealing with visible space proper. The quoted equations are new and possibly better than old ones but, like the latter, they also do not teach us anything about how far $\bar{P}'$ and P_7' (the visual counter parts of $\bar{P}$ and P_7) appear. To explain the perception of the absolute distance of $\bar{P}'$ and P_7', the author finds it necessary to rely on experientialist assumptions. "A person," according to the author, "learns to perceive differences in distance by using his hands to hold one object at the point of fixation $\bar{P}$ and a second object at P_7 and by noting the relation between the disparity of the retinal images of $P_7 \cdots$ and the displacement of P_7 in front of $\bar{P}$ perceived through the hands." This intellectual feat first performed by nearly all in infancy turns the physical distances $O\bar{P}$ and P_7 into distances $\bar{P}'$ and P_7', respectively, of visual space and the equation (4a) of physical space suddenly transforms into an equation in which quantities of physical space figure on one side and quantities of visual space on the other (and one will wonder in what common units such different quantities should be measured):

$$\frac{1}{\bar{\rho}'} - \frac{1}{\rho_7'} = \frac{\bar{\gamma} - \gamma_7}{2a} \tag{5}$$

This learned evaluation of retinal disparities becomes, according to the author, extended upon any point P_1 of the horopter and upon any point P in front or in back of the horopter, as long as both points are situated along the same line SP_1P, a line which forms the angle ϕ with line $S\bar{P}P_7$, the x-axis.

"The next problem is that of learning to evaluate the relative distances of $\bar{P}$ and P_1" (whatever this means). Here the author turns to the use of size constancy. "The brain arrives at its evaluation of P_1' for each of the various radial vectors by reassessing P_1' until objects moving in a fore and aft direction along

each radial vector appear to maintain a constant size in the fore and aft direction." This, of course, might or might not be so and it is hard for this reviewer (who could never quite reconcile himself with experientialist explanations) to believe that the brain could ever accomplish such a task. In any event, the assumption justifies the creation of one of the most interesting equations of this paper:

$$\frac{\rho'}{\rho} = \frac{\rho_1'}{\rho_1} = \sec \phi \left(= \frac{\cos \phi}{1} \right) \tag{7}$$

an equation which relates the objective and visual distances of points on or off the horopter along any of the "radial vectors" (or polar coordinates) emanating from S. (These ϕ-vectors, introduced by Luneburg, are, in this reviewer's opinion, the really isomorphic structural basis of visible and visual space.) Since the secant of $\phi = 0$ is unity, $\bar{\rho}$ and $\bar{\rho}'$ (the physical and visual distances of the symmetrical point of bifixation) are equal. In the case of any other horopter point the brain makes a mistake by the factor sec ϕ, thus peripheral points of the horopter are not actually seen at their "real" distance.

Since the horopter in most authors' opinion (and the author of this paper seems to be one of them) is not coincident with the Vieth-Müller circle (what the criterion of the horopter is, the author fails to reveal), points of it cannot be viewed by the two eyes under a constant angle $\bar{\gamma}$. Each point P_1 is viewed under some different angle γ_1. The angle $\bar{\gamma} - \gamma_1$ which is pertinent to this point cannot actually be called an angle of disparity since each γ_1 of each horopter point P_1 supposedly constitutes the angle between the lines of direction of respective corresponding points. The equation of the horopter is

$$\bar{\gamma} - \gamma_1 = H_1\phi^2 \tag{8}$$

where H_1 is a function of $\bar{\rho}$.

In this equation several changes can be effected. First of all, according to equation (2)

$$\bar{\gamma} = \frac{2a}{\bar{\rho}}$$

and since $\bar{\rho}$ and ρ' have just been shown to be identical,

$$\bar{\gamma} = \frac{2a}{\bar{\rho}'}.$$

Furthermore,

$$\gamma_1 = \frac{2a \cos \phi}{\rho_1} = \frac{2a}{\rho_1 \sec \phi}$$

and from equation (7)

$$\rho' = \rho_1 \sec \phi.$$

Thus,

$$\gamma_1 = \frac{2a}{\rho_1'}$$

Equation (7) can therefore be rewritten in terms of visual rather than physical distances on its left side:

$$\frac{1}{\rho_1'} - \frac{1}{\bar{\rho}'} = \frac{H_1 \phi^2}{2a} \tag{11}$$

and one has, according to the author, the equation of the visual counterpart of the horopter, i.e. of that surface in visual space in which things are seen if they actually are in the horopter. "Essentially the job which the brain must perform is to associate with each value of $\bar{P}'$ [the subjective counterpart of $O\bar{P}$, the point of symmetrical bifixation, the nuclear point of the Heringian nomenclature] a surface of a certain curvature as representing the counterpart of the horopter in visual space and then objects in front or behind the horopter are perceived in relation to the counterpart of the horopter in visual space." As mentioned earlier, the author believes that the absolute visual distance of $\bar{P}'$ is learned by association with tactile sensations. (For Luneburg it was determined by sensations coupled with a certain convergence angle γ and this reviewer too is convinced that the proprioception of convergence is much more likely to determine the sensed distance $\bar{\rho}'$ of $\bar{P}'$ than the length of the outstretched hand touching $\bar{P}$. Whether this association is a learned one is still another question. Unfortunately, we do not learn from this paper how we *know* that things are in the horopter even if we sense how far $\bar{P}'$ is, since the author neglects to tell us anything about the function H_1. Nor does he tell us anything about the objective or subjective criteria which determine that points are in the horopter.)

Further additions to this building of equations follow. One of them, a more general equation,

$$\frac{1}{\rho'} = \frac{\gamma}{2a} + k = \frac{\cos \phi}{\rho} + k \tag{16}$$

relates the sensed distance ρ' of any point P of physical space to the pertinent angles γ and ϕ and to the distance ρ. Another equation refers to the Vieth-Müller circle.

In the case of the Vieth-Müller circle where γ_3 is constant for any point P_3 and identical to $\bar{\gamma}$, it turns out that the general equation (16) reduces to

$$\rho_3' = \bar{\rho}' \tag{18}$$

thus any point of the Vieth-Müller circle appears equidistant—a certainly elegant proof of one of Luneburg's most interesting theoretical deductions (for which, however, experimental confirmation is still sorely lacking).

Another interesting section deals with the analysis of the apparent fronto-parallel plane. For any point P_2' of this apparent plane seen at the distance ρ_2' the following equation is valid:

$$\rho_2' = \frac{\bar{\rho}'}{\cos \phi'} \tag{19}$$

Taking the pertinent physical counterparts to these subjective values and

after some transpositions (which cannot here be reproduced), one gets for small angles ϕ the following equation:

$$\bar{\gamma} - \gamma_2 = \frac{a}{\bar{p}'} \phi^2 \tag{23}$$

in which the term $a/\bar{p}'$ is constant for each of these planes and is called the Hering-Hillebrand deviation coefficient to which considerable study has already been devoted by Ogle (1950). According to the following equation, this coefficient can also be written:

$$\frac{a}{\bar{p}'} = \frac{a}{\bar{p}} + ak \tag{24}$$

(This is a derivation which this reviewer cannot follow since, according to a definition given by the author previously, $\bar{p}' = \bar{p}$ for any symmetric bifixation point $\bar{P}$.) The values of the theoretically derived coefficients should, of course, agree with the experimental values determined by Ogle. (It is hoped that the author will analyze this problem in the near future.)

Following this line of thought, the author finally arrives at the analysis of the fronto-parallel plane of visible space, the equation of which is

$$\rho_4 = \frac{\bar{p}}{\cos \phi} \tag{25}$$

for any point P_4 in this plane—ρ_4 being the distance of P_4 from S. The equation for the visual correlate of this plane becomes

$$\rho_4' = \frac{1}{\bar{p}'} - \frac{\sin^2 \phi}{\bar{p}} \tag{28}$$

since ρ'_4 is greater than $\bar{p}'$, the subjective counterpart of any objective fronto-parallel line must always be a surface convex toward the observer. The amount of convexity will depend upon the perceived distance. "And since the eye must learn to associate certain curvatures with certain distances, perceived curvature and perceived distance become interchangeable quantities." This offers, according to the author, a chance to explain certain visual illusions of distance, like the ones created with the asymmetrical magnifiers invented by the late A. Ames, Jr. (Am. J. Psych. 1946, *59:* 333–357).

ARTHUR LINKSZ

Reports from Abroad

SINGAPORE

Singapore has a population of about 1.2 million, half of which are under the age of 20 years. Apart from two smaller private eye clinics, the Eye Department of the General Hospital is the city's main center for ophthalmic treatment. The department has 80 adult beds and 20 cots, and has an average daily attendance of 100 to 150 outpatients.

During the year 1955, a total of about 14,000 new patients were treated, and the statistics revealed the following salient features: Nearly half of the total were sufferers of conjunctivitis; a good proportion were Koch-Week's type, often affecting whole families of the poorer classes. These numbered 5110 and responded well to daily dabbings of the palpebral conjunctivae with 2½ per cent silver nitrate solution, or to a combination of this treatment with oral sulphonamide drugs. Trachoma was diagnosed in 618 cases by the presence of both pannus and follicles by means of the loupe or the slit-lamp. There were often cases with superadded infection with other organisms. These were treated on the same lines; aureomycin ointment and sulphacetamide drops were given later as a follow-up treatment. Very few cases necessitated expression of follicles, while a fair number of advanced cases needed surgical treatment for marked entropion and trichiasis. A modified method of van Millingen's grafting of buccal mucosa strips to lid margins was performed on 75 cases with uniform satisfactory results.

Phlyctenular disease numbered 428, and was also prevalent mainly among malnourished children of poor families living in unhygienic homes and surroundings. Some of them had tuberculosis. Topical cortisone therapy has diminished greatly the tragedy of extensive corneal vascularizations and scarrings which had previously led to varying degrees of visual loss. The more resistant cases had to be removed from their unhealthy environment by hospitalization at which time they began to respond to treatment rapidly.

There was a high incidence of epidemic keratoconjunctivitis with a total of 507 cases. Practically all were adults. Only very occasional cases were found among the older school boy or girl, but never among young children or infants. The early acute infections are rapidly controlled by the frequent applications of cortisone drops with the complete disappearance of all the tiny superficial infiltrations in the cornea within a few days. However, these infiltrations oftentimes reappear with the stoppage of cortisone treatment and disappear again on resumption of the drops. It is noted that these relapses are usually not accompanied by any acute symptoms. The late untreated cases present a quiet eye with multiple rosette-shaped, fuzzy-edged opacities, 1 to 3 mm. in diameter, scattered over the surface of the cornea. Cortisone has little or no effect on such cases. This disease appears to occur haphazardly among people from many different and unassociated walks of life with no definite traceable epidemic center.

There has been a marked decrease in the number of cases of keratomalacia seen during the past two years. In 1952 there were 62 cases recorded, and in 1955 there were only 5 cases. This decrease in incidence has coincided with the recent fortifications of sweetened condensed milk with the requisite concentrations of vitamins A and D by the manufacturers of the milk brands popularly used by a large section of Asian mothers in the feeding of their infants. It is to be pointed out that the manufacturers started this measure only after the Eye Department had publicly laid the blame of this disease at the door of sweetened condensed milk, all of which were proved by analysis to contain inadequate contents of vitamins A and D.

Pterygium is a common condition occurring mainly among the laboring classes. It bears out to a certain extent the theory that constant exposure to sunlight and dust in the tropics might be the predisposing factor to its occurrence. Patients often have multiple pterygia, and it is by no means rare to see four pterygia in one patient. We employ McReynold's operation as the routine treatment for this condition, and 382 cases were operated on during the year. There were only 5 cases of postoperative recurrence of the growth, and it would appear that there is no very effective method of treatment to prevent further recurrences in a few very intractable cases.

Anterior uveitis cases numbered 192, and a good proportion of these were associated with paranasal sinusitis. Hansen's infection and syphilis accounted for a small number of cases, but no case of iritis has yet been traced to tuberculosis. However, a few cases of choroid tubercles were seen in young children suffering from tuberculous meningitis. The majority of cases were undoubtedly manifestation of bacterial allergy with etiology undiagnosed. Protein shock therapy in the form of intravenous injections of T.A.B. vaccine has proved to be useful and safe. Its use must be limited in cases where contraindications exist.

A very limited amount of refraction work was being carried on by the department among a restricted number of school children sent through the school clinics, which directed the bulk of the cases to practicing opticians in the city. Myopia with or without astigmatism was the most common refractive error found. The record showed 784 of these cases as against 76 cases of hypermetropia. 78 of the myopes had errors of over 7 diopters, while 29 were cases of malignant myopia with extensive degenerative changes in the retina.

There were 24 cases of congenital cataract and 616 cases of senile cataract. A total of 518 cataract extractions were done during the year. Seventy per cent of these were simple intracapsular extractions. We employ as a routine a single McLean's pre-placed corneoscleral silk suture; incision with Graefe knife and the lens delivered by the tumbling method with Arruga's intracapsular forceps. Extractions are performed regularly on three days of the week, and practically no cataract case has to await operation on a waiting list. There were 139 poor patients recommended for free cataract glasses.

Lastly, 142 blind cases were registered for the year. These consisted of 99 totally blind and 43 partially blind. The causes of blindness in the order of frequencies were:

Optic atrophy (mainly luetic), glaucoma, phthisis bulbi, malignant myopia, trachoma, retinitis pigmentosa, keratomalacia, and chronic iridocyclitis.

A school for the blind supported jointly by government and by voluntary donations has just been established for the welfare and education of the young blind of Singapore.

The rather high incidence of acute infective conjunctivitis is striking. Eighty per cent of the population are Chinese, who as a rule favor the bringing up of large families. This infection affects mainly the families of the lower income groups whose numerous members live in markedly overcrowded quarters, have little or no knowledge of personal hygiene and are handicapped by a lack of proper sanitary facilities. It is therefore bound up with the city's progress in housing, health, and education programs. In the matter of treating this condition on a mass basis, we have found for many years that our routine treatment of this condition with silver nitrate in combination with sulpha drug orally when necessary is unsurpassed both in economy and in achieving consistent results.

On the other hand, the incidence of trachoma is comparatively low and it does not present an epidemiological problem. Only the neglected and untreated cases end in lowered vision and blindness. The timely operative treatment for severe trichiasis has lowered the incidence of blindness due to trachoma.

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Eye Department, General Hospital, Singapore

ISRAEL

The incidence of eye conditions in Israel, as do many other of its aspects, reflects both the East and the West. Among its citizens born in the East there is quite a high incidence of trachoma; many a cornea bears the scars of a childhood infection or even perforation; while on the other hand the fundi apparently show a relative freedom from the retinopathy of hypertension and diabetes. This is particularly true of those who have immigrated since the foundation of the state eight years ago. From Yemen, the Yemenites brought an incidence of active trachoma of more than 80 per cent; from Persia and Iraq the incidence was about 20 to 25 per cent, while from North Africa the figure varied from 10 to 25 per cent. Among its occidentally born citizens trachoma varied in its incidence from about 2 per cent among those born in Eastern Europe to practically nil among those from Western Europe and the Americas. On the other hand, these latter groups have their retinopathies in a degree at any rate no less than equal to that prevalent in the lands of their birth. The relative incidence of errors of refraction among the occidental and oriental sections of the community is at present being worked out. Cataract, glaucoma, retinal detachment, and squint are, at least to general observation, fairly well divided among the communities; while corneal opacity demanding graft operation is, as might be expected, more common among those born in the East.

During the last generation great changes have taken place with regard to the seasonal incidence of infective ophthalmias. Koch-Weeks conjunctivitis is certainly on the decrease, while gonococcal conjunctivitis, which for example is one of the main causes of blindness in Egypt, is not seen at all.

To serve the population there are about 100 ophthalmologists, the great majority of whom graduated and received their postgraduate training abroad. The events of 1933 and afterward brought into the country a wealth of knowledge and skill on which is based the present arrangement of services in the country. Most of the population (over 70 per cent) are members of the Central Sick Fund, which has ophthalmic dispensaries all over the country. Cases are for the most part referred for surgery from these dispensaries to one of six hospital centers which are in Tel-Aviv and area, Haifa, and Jerusalem. These centers which have a total of about 200 beds are controlled as follows: three by the government, one by the municipality of Tel-Aviv, one privately, and one by the Hadassah. All these centers are busy hives of surgery. In several of these centers are facilities for orthoptic investigation and treatment. There are only two or three trained orthoptists in the country; there is room in the country for more orthoptists. Consideration is now being given to the organization of such training in Israel. There are glaucoma units in several of the larger centers.

As can be gathered, about 60 per cent of the ophthalmologists in the country have no facilities for doing major surgery and are engaged to a great extent in refraction work. By legal statute inherited from the times of the British Mandate,

all treatment including the testing and prescription of glasses may be done only by registered medical practitioners. The large number of ophthalmologists in the country permits what in other countries may be considered to be a luxury. The relatively small salaries received by ophthalmologists, as by other physicians, prevents this from being a financial burden on the country.

The Ophthalmological Society of Israel has been in existence for over 25 years. Clinical meetings are held every two months in one of the main hospital centers of Jerusalem, Haifa, or Tel-Aviv and its neighborhood. These meetings usually have an attendance of about 80 per cent of the membership of the Society. In addition to the demonstration of cases there is a program of lectures which are transacted in the Acta Medica Orientalia. The proceedings of the meeting are all conducted in Hebrew, although the transactions are reported in English. Although Hebrew has been expanded only within the recent decades so as to serve the needs of science, it fluently conveys the necessary conceptions of ophthalmology. At these meetings one never ceases to wonder as speakers having recently come from more than a dozen countries expound with a lucidity varying, of course, with length of stay in Israel, but always sufficing to enable business to proceed with ease. In this connection an important educational role has been played by Aryeh Feigenbaum, scholar and linguist and first occupant of the Chair of Ophthalmology in the Hebrew University of Jerusalem. He has published a textbook in ophthalmology which is in general use.

Undergraduate teaching in ophthalmology began in the Hebrew University in 1951. It consists of the following: in the fourth year of studies (first clinical year) each student has 10 hours' instruction in the use of the ophthalmoscope as part of general instruction in physical methods of diagnosis. The purpose of this is to permit him to begin the examination of the fundus of the eye as soon as he begins his training in general medicine, a facility which would otherwise have to be deferred until the sixth year of the training when the systematic course in ophthalmology is given. The systematic course consists of 20 didactic lectures and 45 to 48 hours of clinical demonstration.

Research has its devotees and during the past few years work has been published on (1) The presence of complement-fixing antibodies to the group specific antigen of the psittacosis lymphogranuloma venereum group in the sera of trachoma patients. (2) Changes in the conjunctival vessels in diabetes and hypertension. (3) Factors affecting new vessel growth into the cornea. (4) The assessment of hyaluronidase in the eye. (5) Growth of iris in tissue culture. (6) The pathogenesis of retrolental fibroplasia. (7) Glucose utilization of the retina. (8) The pathogenesis of retinal hole. (9) Disturbances in scotopic vision in pregnancy, climacteria, oligospermia and in adposogenital dystrophy. (10) Studies on antigens in the human cornea.

A research laboratory is attached to the ophthalmic department of the Hebrew University with a section dealing with histology, experimental pathology, biochemistry, and electric physiology of the eye.

I. C. MICHAELSON

Book Reviews

"Surgery of the Eye: Diseases," by Alston Callahan (*Charles C Thomas. Cloth. $25*), *is a monumental discussion of surgical techniques. It is reviewed by Saul Sugar, who is the author of "The Glaucomas."*

By Saul Sugar

As new methods are devised by ophthalmic surgeons and appear in the literature, it becomes necessary, from time to time, to organize and evaluate them. In this outstanding book, Callahan has not only brought together the most up-to-date methods of ophthalmic surgery but he has added a good number of his own and presented them in an ideal manner—with concise technical descriptions and superb large drawings of the various stages in the operative procedures.

Beginning with a chapter on anesthesia, a sound up-to-date approach is used. Controversial methods are avoided and the best in the author's experience is presented.

The chapters on lid diseases are outstanding. Of the congenital anomalies the treatment of epicanthus is excellent. Different procedures are advised for the various types of epicanthus. The use of scissors instead of a knife in making the Z-plastic incisions is advised. A definition of blepharophimosis might have been incorporated into the discussion of this subject.

In discussing the operations for blepharoptosis, the description of the Blaskovics-Berke operation is exemplary. Particular emphasis is placed on the technical details. The Berke-Motais operation is the preferred superior rectus type of procedure. A modification of the Friedenwald-Guyton suture is described.

Senile entropion is classified on a physiologic pathology basis into spastic, relaxed, and cicatricial senile types. Callahan describes his method of dissecting and bisecting a band of Riolan's muscle in the spastic type. The two ends are then crossed and the ends attached to the tarsus near the lid margin with white silk or cotton. For the relaxed type, the Fox procedure is advised. The senile cicatrical type is best corrected with Wies' method. For the usual cicatricial entropion which is distinguished from the senile type, the Lagleyze procedure is preferred.

Senile ectropion is similarly separated into relaxed, cicatricial and spastic types. For the first the Kuhnt-Szymanowski method and for the second the Stallard bridge pedicle flap are used. Callahan used his method of removal of orbicularis from the middle third of the lid for the spastic type. In describing lateral angle tarsorrhaphy, there is no mention of an incision in the lower tarsal tongue which is shown in the photograph. There are few other omissions or errors in this remarkable book.

Reconstruction of the lids following removal of malignant tumors is based on the size of the defect. Where only one-fourth of the lid margin is involved,

Wheeler's halving procedure is used. When between one-fourth and one-third of the margin is involved, the lower arm of the lateral canthal ligament is relaxed before using the Wheeler method. When one-third of the lid margin (except the nasal third) needs reconstruction a pedicle flap is used. When one-half the lid is to be reconstructed, Callahan's techniques are described. For lesions of the entire lower lid the Hughes procedure is used.

Callahan has devised a procedure for blepharochalasis utilizing orbicularis to form imbricated supportive layers after removing hermeated fat.

Diseases of the lacrimal apparatus are systematically considered. A diagnostic examination procedure to determine the site of obstruction to lacrimal drainage is outlined and the various surgical procedures described. For eversion of the lower punctum Callahan advises the Blaskovics operation for those everted by relaxation and Lee's method for cicatricial eversion. When the canaliculus is involved in a neoplasm the uninvolved canaliculus is opened through and united to the conjunctival mucosa so that the drainage is not interfered with. For closure of the canaliculi in keratoconjunctivitis sicca diathermy coagulation of 6 to 7 mm. of the canaliculi is done and a 2-mm. section of it removed and the ends sutured. The use of acrylic tubes is described and proper warning of the chances of failure is given.

The sections on cataract are excellent and cover the many complications and methods of handling them. Particularly valuable are drawings of techniques used for cataract extraction in various parts of this country.

In the section on secondary glaucoma Callahan states, and the reviewer agrees, that removal of the lens in glaucoma capsulare does not relieve the cause of the glaucoma. However, he states that "it was formerly assumed that the increased pressure of glaucoma capsulare was caused largely by the particles of the lens capsule falling into the anterior chamber." Actually this assumption has not been disproved.

In the section on primary glaucoma Callahan lists the various indications for surgery, a total of 25, including four special problems. For many, this will be of great help, but is, perhaps, an oversimplification of what is very much an individual problem. The operative procedures include the anterior flap sclerotomy with basal iridencleisis of Stallard. Here again, the drawings are excellent. Callahan's method for repairing a cystic or perforated trephine bleb is to be recommended.

The chapter on orbit considers tumors of the orbit and methods of surgical removal. The Berke modification of the Kronlein operation is well illustrated.

An appendix contains two fine chapters on advances in management of injuries of the eye and of the ocular adnexa.

The author is to be congratulated on this excellent book, as are the artists and publisher. It is recommended as a textbook for the eye resident as well as for the experienced ophthalmic surgeon.

"Biochemistry of the Eye," by Antoinette Pirie and Ruth van Heyningen. *(Charles C Thomas. Cloth. 323 pp. $7.00) is the first book in the field for many years. David Shoch, who reviews it here, was a biochemist before studying medicine.*

By David Shoch

Few disciplines (except nuclear physics) have advanced as rapidly as biochemistry in the last two decades. The application of the advances in this field to ophthalmology has been rapid and successful, and the authors of this excellent text have been in the forefront of the relatively small group that has sparked this fruitful liaison.

This book is particularly timely. Duke-Elder, Vol. I, and Krause's "Biochemistry of the Eye" are over twenty years old, and although Adler discusses many biochemical processes in the eye, the need to cover all of clinical physiology of necessity limits the space for presentation of pure biochemistry. Pirie and van Heyningen have covered the complete eye, but their first love is the lens, and about one-half the text is devoted to this organ. This is justifiable, both from the authors' and the reader's points of view. Cataract is probably the most frequent pathologic change seen by the ophthalmologist, and it is the field in which the writers have been most prolific. Their work has been ingenious and careful, yet it is presented in a lucid and simple style which makes even so complex a subject as glucose metabolism comprehensible to the clinical ophthalmologist. The literature is well covered, although it is selective and critical, rather than comprehensive. (A recent monograph on the lens by Jean Nordmann entitled "Le Biologie du Cristallin" is all-inclusive and thus complements the present text nicely. It is unfortunately available only in the original French.)

The second half of the text is devoted to the biochemistry of the cornea, vitreous, retina and aqueous. The authors point out that they have intentionally been brief in these sections because many good reviews are available elsewhere. One can only wish they had been less modest and lent their talents for description and clarification more fully to these structures as well as to the lens.

In summary, this book is a "must" for every research worker in ophthalmology and is strongly recommended to the clinician who has any interest at all in ophthalmology beyond dispensing spectacles and the latest cortisone preparation.

Current Review

A RESUMÉ OF CROSS CYLINDER APPLICATION AND THEORY

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A modest estimate of the number of papers written about the cross cylinder since its first application by Jackson, would be about 50. However, a complete description of all its uses never has been assembled nor have the various controversies concerning the technique of application of its optical effects in refraction been presented.

All would agree that most time in refraction is occupied with determining the amount and axis of astigmatism. Years ago Crisp[1] wrote that 97 per cent of his refraction patients required a cylinder in one or both eyes. In this respect, times have not changed.

BRIEF HISTORY

Stokes, an Irish scientist, first introduced a type of cross cylinder to European ophthalmologists in 1849.[2] Later, 1885, Dennett brought it to the United States, but it was never received with enthusiasm in its form and use at the time. Indeed, its use scarcely involved more than trying individual cylinders before the eye in various strengths and axes.

Practical, clinical application of the cross cylinder was first made by Jackson in 1887 in the *Transactions of the American Ophthalmological Society*. At that time he used it for the measurement of astigmatic power only. It was not until 1907 that he described its use for determining the axis of a cylinder.

Surprisingly, Jackson was not a prolific writer concerning the cross cylinder. Description of its attributes fell into the capable hands of Crisp who diligently and forcibly brought the little device to the attention of the ophthalmologic world both here and abroad.

NATURE OF THE CROSS CYLINDER

The cross cylinder consists of a plus cylinder and a minus cylinder of equal strength crossed so that their axes are at 90 degrees to each other. Such a lens is ground as a concave sphere and a convex cylinder of twice the power of the sphere.[3] It is mounted in a metal frame with the handle placed at exactly 45 degrees to the two crossed axes of the cylinders. The lens should be ¼ to ½ inch larger than a trial lens;[4] therefore it is usually made 1½ inches in diameter.

Several strengths of cross cylinders are made, −0.12 D. Sph.⌒ +0.25 D. cyl., −0.25 D. Sph.⌒ +0.50 D. Cyl., −0.50 D. Sph.⌒ +1.00 D. Cyl., −1.00 D. Sph.⌒ +2.00 D. Cyl. Respectively, these are called a 0.12 D. cross cylinder,

a 0.25 D. cross cylinder, etc., depending on the resultant power of the cylinders incorporated. More recently a 0.37 D. has been placed on the market. If a cross cylinder of greater power than the ones manufactured is needed it can be improvised from the trial case. Jackson[5] used the 0.50 D. cross cylinder most and said the 0.12 D. was virtually useless. However, some refractionists say they get excellent results with the 0.12 D. cross cylinder. Today the one most commonly used probably is the 0.25 D.

The general opinion seems to be that the poorer the vision, the higher the power of cross cylinder used. For instance, for aphakic eyes, Crisp[1] recommended the 1.00 D. cross cylinder. Lancaster[6] used an 0.50 D. cross cylinder when the test cylinder was strong. Pascal[7] apparently disagreed with these general principles, saying he used as strong a cross cylinder as the error of astigmatism being tested.

Friedman[8] wrote a critique of the cross cylinder some years ago explaining how its chief uses could be duplicated easily with ordinary trial lenses. This opinion appears to be at variance with that of all who have written on the subject.

A common practice is to use the higher powers of cross cylinder, 0.37 D. and 0.50 D., in "roughing out" the refraction. Then as the vision improves with various changes of lens the 0.12 D. and 0.25 D. are used. For aphakia, poor vision and high cylinders, the 1.00 D. is used.

Unless otherwise stated all cross cylinder tests are done with one eye occluded.

QUESTIONING THE PATIENT

Each refractionist undoubtedly will develop his own method of interrogating the patient while using the cross cylinder, especially as experience increases. The author, placing the instrument before the eye, says, "Now this doesn't help," and as he flips the instrument, "neither does this—but which side is better?" This is not strictly true, for occasionally the patient will state triumphantly that one side or the other does help, but my method is timesaving to me. As I keep changing the lenses or the axis I usually explain that the end of the test comes when he cannot tell the difference in blurring. Many ask the patient which blurs the most. Some[9] have the patient close the eye between each flip of the instrument.

Lancaster[6] asked the patient if he could read smaller letters as he changed the cross cylinder. Almost all advocate that the alterations should be made quickly and the patient should be required to answer promptly. He is not expected to render a considered judgment with each flip of the instrument but to give his instantaneous impression. However, Crisp[10] stated that in the final stages of refraction when the patient was in doubt he insisted that the patient read more letters one way or another. The author does not agree with this. When the patient is in doubt, that is the end of the test—the point we strive for. In other words the patient cannot tell you which is better or worse. Lindner[11] and others emphasized the value of the suddenness of change rendered by the quick flip of the cross cylinder. Hildreth[12] said that in this sense, speed favored accuracy.

Jackson,[13] to give objective value to subjective testing, stressed the idea of repeated tests both the same day and on different days.[4] Incidentally, he said he held the cross cylinder an "inch or two" in front of the trial lens. I doubt if he ever held it at the latter distance since it is very difficult to align properly and there is no reason optically why it should be done so.

Most examiners instruct the patient to look at the smallest line of letters that he can see. Almost invariably, in my experience, the patient then directs his attention to a line smaller than he can read. It seems best to direct his attention to a line you know he can see; therefore, when I know the patient is trying to read the 20/15 line I direct him to gaze at the 20/20 or 20/25 line, asking him which change of the cross cylinder is "better." In a test of this type where the quick impression probably results in a more accurate answer than studied thought, it seems best to reserve the meditation until the last 0.12 D. to 0.25 D. have been added to the prescription and we are testing for final visual acuity.

If, for any reason, the examiner is dissatisfied with the patient's answers, he should have him look at a larger line of letters, such as the 20/30 or 20/40 line. Sometimes it is easier for the patient to reach a quick decision while looking at such large letters.

CYCLOPLEGIA AND FOGGING

Jackson[5] said that the best test for astigmatism without cylcoplegia was with the cross cylinder, but at the same time he indicated that the cross cylinder test was done best under cycloplegia with the pupil dilated 4 mm. or more. Almost all authors agree that, at least in selected cases, there is no substitute for cycloplegia and retinoscopy in assisting the examiner to determine accurately a refractive error, no matter what additional aids are utilized.

Cowan, discussing Halper's[14] paper, also states that the cross cylinder test is best done with cycloplegia, although Roveda[15] maintains that the cross cylinder has a minimal effect upon accommodation.

According to those who studied with Jackson,[16] he used his cross cylinder tests with the eye in a fogged condition. Jackson himself[4] indicated this in one of his treatises on the subject. There is no question that he also used it in the final tests with the eye seeing its best.

On this point Crisp[3] hedged a little with the following statement: "Like all other astigmatic tests, this one is more likely to be successful if the accommodation is relaxed, and therefore, if whatever spherical lens in the trial frame is so strong a plus or so weak a minus as barely to allow the patient to obtain his full visual acuity." In another article[17] Crisp stated that during the test the eye is not "appreciably fogged."

Lancaster[6] used fogging when testing for both power and axis; Friedman[8] did likewise, stating, "In all instances in which the cross cylinder is employed, except in determining presbyopic error, it is recommended that the patient's vision be fogged with a +0.25 D. or +0.50 D. sphere."

Pascal[18], I believe, was the first to point out that when the eye is ". . . tested with usual test-types where vertical lines are more prominent than horizontal,

the patient when partially fogged, tends to choose too great a cylinder against the rule." He was referring to the cross cylinder test for power.

It seems to have been generally agreed that test letters are more legible when their vertical components are clear and their horizontal components blurred than vice versa.

In several statements[7, 19] concerning the cross cylinder, Pascal brought forth the idea that the test for power is done best with the eye in a state of "meridional balance" or in a mixed astigmatic condition.

This means that during the refraction the retina, by the use of plus and minus spheres, is kept in Sturm's interval so that the patient can at all times compare diffusion circles instead of elliptoids whose axes are at opposite meridians. In other words, one principal focus of Sturm's conoid lies in front of the retina and one behind. If this is not done the patient may state that he sees different kinds of blurring when the examiner flips the cross cylinder and that he cannot adequately compare them. Smart's explanation[20] of the mixed condition in relation to the cross cylinder is excellent.

Pascal always maintained that when the eye was fogged, when testing amount of astigmatism, even to a slight extent, the results of the cross cylinder test were most likely to be indefinite and misleading.

Williamson-Noble[21] in 1943 wrote an illuminating article on the subject of fogging when using the cross cylinder test for power. Using a camera, lenses and test-type he showed conclusively that fogging causes a patient to choose too much cylinder against the rule and vice versa. Reviewing this essay editorially Crisp[22] agreed.

Williamson-Noble, like others before him, emphasized the importance of keeping the eye in a mixed condition when testing for power especially when the axis is within 20 degrees of the vertical or horizontal meridian. Almost all authors appear to agree that where the astigmatism is oblique, in testing for power, a fogged condition of the eye causes less confusion to the patient and examiner.

"Elongation of test letters can be avoided by establishing meridional balance. When astigmatism is present all refractive errors can be reduced to a mixed astigmatism by the addition of plus or minus spheres," wrote Puntenney[23] in his paper on the cross cylinder.

Martin[24] believes that during the test for power, hypermetropia should be under-corrected and myopia over-corrected less than 0.50 D. But Williamson-Noble states that such a procedure causes the patient to choose too strong a cylinder with the rule and vice versa, that is just the opposite fault from the effect of fogging.

Little has been said on the exact procedure employed in keeping the eye in a mixed condition except by "the use of plus or minus spheres." Then how does the student know when the eye is in a "mixed condition?" Williamson-Noble uses the duochrome test several times during his refraction. If the patient sees the test letters against a red or green background equally blurred or equally well defined, he knows the condition is mixed. If the red seems more blurred he adds a small plus sphere, if the green, a small minus sphere. He then returns to the black and white letters using the cross cylinder.

Pascal[7] used the correcting cross cylinder, more of which will be mentioned later, to maintain a mixed condition. Testing as he described must be a very laborious process, for apparently he not only changed spheres and cylinders where necessary but also changed the power of the correcting cross cylinders and testing cross cylinders numerous times during a refraction.

It seems to me that for a test whose greatest merit is rapidity and simplicity, a great deal of perhaps useless detail has been added, that is, from a purely practical standpoint. In the first stages of a refraction there are times when the busy refractionist may not be sure that the patient is undercorrected or overcorrected for hypermetropia, for instance. Yet the cross cylinder seems to give excellent results, especially if repeated tests are done and on different days as recommended by Jackson.

I use a cycloplegic on almost all patients under 40 years of age and a mydriatic (so-called as apparently there are none which do not have some slight effect on accommodation) on those above 40 years of age. After retinoscopy, I put the exact prescription in the trial frame, and proceed with the cross cylinder tests. I repeat all cross cylinder tests if possible on another day with the pupil normal. The nearer we come to the exact refractive error, the more valuable and sensitive the test becomes for we then approach the "mixed condition" explained before. The test should be made so rapidly, in my opinion, that accommodation becomes negligible.

DIALS VERSUS CROSS CYLINDER

Very often when the subject of the cross cylinder is discussed, its efficiency is compared to astigmatic dials. Needless to say, there is no reason why an able refractionist cannot use both methods of testing astigmatism. However, there have been several outstanding champions in both camps, their work thought-provoking and interesting. Crisp[2] emphatically stated, "There are many cases where the astigmatic dials are unsatisfactory and unreliable." The remarks by many refractionists lead me to believe that the great majority support this statement.

Lancaster's[6] experiment, using the astigmatic dials and then the cross cylinder for the determination of astigmatic power and axis on the same patients, is instructive and apparently unbiased although he used the Lancaster-Regan dials for years. He found that there was no difference in the axis in 62 per cent of the cases and not over 5 degrees' difference in 74 per cent. In the tests for amount of astigmatism there was not more than 0.25 D. in 96 per cent. This speaks well for both tests. Lancaster believed the dials were best. Beach, in discussing the paper, said, "If trial characters for the cross cylinders are intelligently selected, and if too much reliance is not placed on the astigmatic charts in cases of irregular astigmatism, these two tests take their place among the most delicate and useful that we have."

After reading many papers and texts that touch on the controversy, I have the very definite impression that the great majority of ophthalmologists believe that the cross cylinder is satisfactory in almost all cases and that the dials are unreliable in many cases.

Smart[20], in a carefully prepared and scientifically presented paper, noted that larger astigmatic errors can be corrected by almost any method. He suggested that in the final stages of a refraction the superiority of the cross cylinder technique increases. His work indicates that the cross cylinder test for axis is 3 to 4 times more sensitive than any other test, and for power, 2 to 2½ times more sensitive. Pascal[6] stated that, "When the eye is in a mixed condition (that is, when the patient has mixed astigmatism) the test with the line chart is definitely misleading."

Although I use both the Lancaster-Regan dials and the cross cylinder, were I to be deprived of either, I would instantly choose to keep the cross cylinder. In using the dials, the instruction to the patient, especially if he is not too acute mentally, seems laborious. Getting up to point to the dials is tiresome and time-consuming. However, the two methods are not mutually exclusive. I find I have no excess knowledge or methods in testing astigmatism. At times, all possible clues are helpful.

TEACHING THE USE OF THE CROSS CYLINDER

Testing with the cross cylinder is ridiculously easy to do but absurdly difficult to describe on paper. A student who has never used the instrument and wishing to learn from various expositions in standard texts is very apt to become somewhat confused. The terms of explanation—pluses, minuses, trial cylinders, cross cylinders, various axes of both, turn, rotation, flip, twirl, etc.—become a confused hodge-podge of words.

In this review the words "flip" and "twirl" will be reserved for the motion imparted to the knurled handle of the cross cylinder by the fingers; the words "turn" or "rotate" will be used for changing the trial cylinder or cross cylinder to a new axis.

In describing the test for axis we may say that the handle of the cross cylinder is always held parallel and coinciding to the axis of the trial cylinder, that is, with the two axes of the plus and minus cylinders in the instrument at 45 degrees to the axis of the trial cylinder. This is the "oblique setting" of Pascal which seems an excellent expression to adopt.

In describing the test for power or amount of astigmatism one axis of the cross cylinder is always parallel to the axis of the trial cylinder, the handle therefore always being at 45 degrees on either side of the trial cylinder. This is the "principal setting" of Pascal which likewise shall be adopted.

In demonstrating the use of the cross cylinder I have created an imitation plastic trial cylinder, cross cylinder and trial lens all appropriately marked. They are roughly 2 feet in diameter. Another such aid[25] was recently pictured in the *American Journal of Ophthalmology*, which is in use at the School of Aviation Medicine. Small mock-ups are worse than none and should not be used. Any used for teaching should be large enough so that the plus and minus signs are legible in a large school room.

Jackson suggested that a student could teach himself the technique of using the cross cylinder by manipulating it before his own eye. Such a procedure may

help him to understand its effect after he has learned to use it, but it may only confuse him otherwise. Keeping the various axes properly aligned is impossible; trying it myself convinced me. My own advice to students is to obtain a brief explanation from a refractionist, then watch him use it several times. Reading about it, of course, will help immeasurably.

TO DETERMINE AXIS OF CYLINDER

By far the greatest advantage in using the cross cylinder is in determining the proper axis of cylinder correction. This test should be done before the test for power is done.

The action of the cross cylinder in testing for axis is based upon the behavior of obliquely crossed cylinders. Suppose, for the moment, the minus cylinder was removed from a cross cylinder, leaving only the plus cylinder. Now if the instrument is twirled in the oblique setting before a +1.00 D. cyl. x 90, there would be obliquely crossed plus cylinders, no matter which way the cross cylinder was flipped. When cylinders of like sign are crossed obliquely a new axis is formed between them. In the case just cited, the patient simply indicates which new axis he likes when the examiner obliquely crosses a plus cylinder in the cross cylinder before the patient's plus cylinder in the trial frame.

Crossing the two plus cylinders obliquely causes the formation of a weak sphere which Friedman[8] states is practically neutralized by the sphere in the cross cylinder and may be disregarded.

Pascal[26] stated that for the axis test it is best if the eye is fogged. He believed the effect of the cross cylinder is to distort the retina image spots, and if the position of the axis is incorrect, the cross cylinder distorts them more in one position than in the other. The opinion of most writers and my own experience leads me to use the cross cylinder test for axis with equal success with the eye either fogged or unfogged.

What is the technique of the cross cylinder test for axis? A plus or minus cylinder, depending upon which is used, is placed in the trial frame. The approximate axis is known by: retinoscopy, astigmatic dials, the old prescription, cross cylinder tests for presence of astigmatism, trial and error, etc. We estimate the strength of cylinder in the same way.

In explanation of this technique, it is best to use an illustration. Place a −1.00 D. cyl. x 180 in the trial frame before the patient's eye instead of at the proper axis of 165 degrees. (For clearer understanding the reader should have a trial frame before him.) When using minus cylinders to refract, I pay attention to the minus sign or signs on the cross cylinder, if plus cylinders, the plus signs on the cross cylinder. For me this avoids confusion.

Now place a 0.50 D. cross cylinder in the oblique setting. In this particular case the handle of the cross cylinder held by the examiner will be extended out from the patient's face at 180 degrees, parallel with the floor. Direct the patient to look at the lowest line of letters he can read, then twirl the cross cylinder, holding it steadily in place. First the minus red sign on the cross cylinder lens is above, then below, the handle, or vice versa. In this instance the examiner is

gazing at the cross cylinder signs nearest the handle. To make it clearer, the red minus is nearer the ceiling until suddenly the cross cylinder handle is twirled and the white plus mark is nearer the ceiling. As the cross cylinder is flipped the patient is asked which is clearer, which more blurred, or if there is any difference in visual acuity. In this case, when the minus red mark of the cross cylinder is toward the floor the patient immediately states that he likes this position better.

It is now known that the trial cylinder must be turned toward 175 degrees. How much to turn is not known so it is estimated. Thus it is turned to 175 degrees, the oblique setting is aligned again, and the test is repeated. Once again the patient prefers the position of the cross cylinder with the red minus mark down. Knowing that the trial cylinder has not been turned far enough, it is turned to axis 160 and the oblique setting again is aligned. This time the patient prefers the position of the cross cylinder with the red minus mark toward the ceiling. It is now evident that the trial cylinder has been rotated too far; therefore its axis is placed at 165 degrees and tested again. This time the patient cannot tell which position of the cross cylinder causes the most blur. The test is complete; the proper axis is 165 degrees.

Occasionally a patient is found who will keep saying that one position of the cross cylinder is clearer until the examiner turns the trial cylinder through 180 degrees. This always seems to occur with a 0.25 D. cylinder in the trial frame. Increasing the power of the trial cylinder to 0.50 D. temporarily will improve the results.

With an indecisive patient we sometimes wonder if he really sees the letters with equal blurring. If such is the case, turn the axis of the trial cylinder off 10 degrees both ways and test with the cross cylinder both ways. If the original axis was correct the patient will respond properly.

TO DETERMINE THE AMOUNT OF ASTIGMATISM

The effect the spherical element of the cross cylinder produces in testing for power or amount of astigmatism is the subject of considerable controversy. Generally speaking, the basis of the test is the improvement in visual acuity produced when a cylinder is placed before the eye with its axis parallel to the axis of the refractive error. The author, in testing for power, ignores the changes in sphere as related to the change in power of cylinders. Especially in the final stages of refraction, very often the patient indicates by his answers and visual acuity (which after all is the final arbiter in refraction) that he desires a change in cylinder but not in sphere.

In testing for power, the axis of the trial cylinder is not changed. The power of the first cylinder to be tried is estimated by the same methods outlined previously for determining the approximate axis.

As in the cross cylinder test for determining axis, the patient is warned that neither side of the instrument may be as clear as without it altogether. Especially is this true as the end point of the maneuver is approached.

The following point has been touched upon but it bears repetition. Crisp[1] states, "In the final refraction, and where the axis of astigmatism is nearly or

quite vertical or horizontal, the test for strength is sometimes fallacious, in that the patient tends to prefer the position of the cross cylinder which produces a vertical rather than a horizontal distortion of the letters." Even without fogging this statement seems to apply. For this reason tests with the cross cylinder show a tendency to favor less plus cylinder with the rule and more plus cylinder against the rule. Therefore it is well to remember that during the final maneuvers with the cross cylinder when testing for power, the patient with a +1.00 D. Cyl. x 90 in the trial frame, may incorrectly favor a +0.75 D. Cyl. If at axis 180 he may favor mistakenly a +1.25 D. Cyl. If the examiner is in doubt, he should make the changes which the patient indicates he wants in order to determine if this gives him better vision. As has been stated before, visual acuity is the final arbiter.

FOR DETERMINING PRESENCE OF ASTIGMATISM

Jackson[5] first mentioned that the cross cylinder could be used for determining the presence of astigmatism, especially if all other methods still left the examiner in doubt. The test is simple. The cross cylinder is placed before one cell of the trial frame, with its plus cylinder at 90 degrees. The plus is then flipped to 180 degrees as the patient is looking at a legible line of letters. If he announces equal blurring there is no astigmatism in either of these axes. Next, the plus cylinder of the cross cylinder is rotated to axis 135 and the maneuver is repeated, this time flipped to axis 45. If he again indicates equal blurring there is likewise no astigmatism in either of these axes. However, if he prefers the minus better at 45 than at 135, place a −0.25 D cylinder in the trial frame at axis 45 and proceed to test for axis and strength as described previously.

This maneuver can be done at other meridians but I do not find it necessary. Customarily I use the test during the final check where I am doubtful if a plain sphere exactly corrects the refractive error.

THE CROSS CYLINDER FOR COMPLETE REFRACTION

Naturally, this question is inextricably bound with the one, "Do we change the sphere as we change the cylinder and what effect does the spherical element of the cross cylinder exert when using it in testing for power?" Although Jackson and Crisp never mentioned such a procedure, some writers and teachers have expounded the proposition that for each 0.50 D. change in cylinder made during a refraction there must be a compensating 0.25 D change in sphere, plus with minus and vice versa. In other words, if a +1.00 D Cyl. x 90 is decreased to a +0.50 D. Cyl. x 90 a 0.25 D. sphere must be added to the combination. From this proposition they have gone a step further to say that the entire refraction can be done with the cross cylinder.

Writing on this point, Jackson[27] said: "Such a lens placed before the eye, separates the cylindric effects from spheric refraction, and allows the measurement of each before the other has been fully worked out. . . . The convex and concave cylinders in the trial case change the plus and minus spheric effect, and confuse it with the changes sought by change of cylinder. The cross cylinder, whatever way

it may be turned, leaves the general plus and minus before the pupil exactly the same. *The change of vision it produces is entirely by change in cylinder.*" (Italics author). So far as Jackson was concerned that settled the matter, although he offered no proof in his writing.

Hymes[28], in a splendid essay on the use of the cross cylinder, says: "It has been taught that the cross cylinder may be used to build the sphere of a refraction as well as to determine the correctness of the spherical addition in presbyopia. At first glance, this would seem to be true because of the action of the spherical component of the cross cylinder. However, to add or to subtract from the sphere, one leaves out of account the action of the cylindrical component of the cross cylinder. It must be remembered that the cross cylinder acts at right angles to both its components. It converges rays in one meridian and diverges them equally at the opposite meridian simultaneously. The patient with the emmetropic eye will respond that the cross cylinder causes equal blurring in all meridians, while the patient with a +0.25 D. Cyl. at 90 degrees states that vision is less blurred when the plus component of the one-fourth diopter cross cylinder is held at 90 degrees than it is when the plus component is at 180. The reason is that the horizontal rays, in such an eye, are focused behind the retina and the plus component of the cross cylinder at the 90 degree axis converges them directly upon the retina, while the minus of the cross cylinder diverges the vertical rays behind the retina. Thus, only the vertical rays are out of focus, while if the cross cylinder is held with the minus component at the 90 degree axis, the horizontal rays in this eye are diverged still further behind the retina while the vertical rays which formerly focused directly upon the retina are now converged in front of the retina. From this it follows that one may not add or subtract from the sphere as a result of cross cylinder testing, as the cross cylinder test is simply one of comparison of diffusion images."

Crisp[29] flatly stated that the cross cylinder has absolutely no spheric effect upon the refractive error.

However, as authentic and convincing as these opinions should be, Cowan[30] states, "We are able to add either positive or negative cylindric power and at the same time reduce the spheric power in the same proportionate strength. This differs from the use of plane cylinders for the same purpose."

Morrison, in commenting on Hymes' paper, agrees with this opinion, stating in substance that whenever he reduces the cylindric power he adds half the amount to the sphere and when he increases the cylindric power he subtracts half the amount from the sphere.

Prangen[31] said: "When it is used for strength the cross cylinder alters both the sphere and the cylinder and this alteration should be visualized. If the cylinder effect alone is thought of and the cylinder is changed without the sphere being checked, an increasingly distorted image will be produced and the interval of Sturm will be exaggerated instead of corrected."

Obviously, as Hymes emphasized, there cannot be two different but correct answers to one geometrical problem. One answer is bound to be wrong.

As indicated before, there are innumerable instances when the patient will

choose a change in cylindric power but not a change in spherical power. So far as the author is concerned this is the most convincing and practical proof needed. If this was not believed, then a change in sphere would be made regardless of visual acuity!

In an emmetropic eye the cross cylinder creates a conoid of Sturm, one focal line before the retina and one behind with no spherical effect. Used in a refraction, its focal lines may change positions but its net effect, never. If its effect were partly spherical how could the patient's image ever be equally blurred when the instrument is flipped before the eye?

Additionally, there are instances when the sphere and cylinder have been underestimated by retinoscopy and in the final stages both must be increased. I do not, therefore, use the cross cylinder to arrive at the sphero-cylindric combination.

USE IN PRESBYOPIA

This test was first described by Jaques, an optometrist, and has been used almost exclusively by optometrists for both monocular and binocular testing. The Jaques blur point card is used as the target. On the card is printed a cross whose arms are about an inch long. Each arm of the cross is composed of three heavy lines.

In describing this test Friedman[8] states: "The full distance correction is placed in the trial frame and in front of this a 0.50 D. cross cylinder. . . . For convenience the cross cylinder is bound in the standard trial lens rim with a short handle. It is assumed that the minus cylinder is set at 90 degrees and the plus cylinder at 180 degrees, and the patient is asked whether the vertical or horizontal lines of the cross are clearer. If the target distance is conjugate with the retina, the vertical lines will fall as far behind the retina as the horizontal lines fall before it and the components of the cross will be equally clear. If the eye is presbyopic the vertical lines will fall farther behind the retina than the horizontal and the horizontal arms of the cross will appear blacker. If the patient is overcorrected in his reading addition the horizontal lines will fall farther in front of the retina than the vertical, and the vertical arms will appear blacker. The requisite strengthening or weakening of the plus sphere is made to equalize the clarity of the cross arms." Halper's[14] description of the test is quite similar.

Hyme's remarks[28] concerning the test are as follows: ". . . Cross cylinders refract rays as cylinders and not as sphere and cylinder. Thus the combination of -0.50 D. Sph. $\bigcirc$ $+1.00$ D. Cyl. x 90 refracts rays as a cross cylinder, the -0.50 D. sphere diverges rays at all meridians and the superimposed $+1.00$ D. Cyl. x 90 converges all horizontal rays to an equal distance in front of the original point of focus. Thus only the vertical rays continue to be diverged by the -0.50 D. Sph. In other words, the function of the minus sphere has been changed to a minus cylinder. One cannot employ a simple cylinder to test the accuracy of a sphere."

Although Hymes' conclusions seem incontrovertible on theoretical grounds

practically, the test appears to be as reliable as any. Binocularly, the more I use it the better I like it.

A few years ago Goldberg designed a blur-point card of his own on which is printed a red and green cross used similarly to the black cross. Exact instructions for its use are printed on the reverse side of the card.

THE CROSS CYLINDER WITH ASTIGMATIC CHARTS

The cross cylinder may be used with astigmatic charts to test both for power and axis. The tests are all somewhat similar in that the end point of all such procedures requires that the lines of the astigmatic charts be seen by the patient as equally uniform in blackness, or that any variation in intensity be equal with alternate flips of the cross cylinder.

Apparently Crisp[32] was the first to use such a test. He utilized it for amount of astigmatism only. Later[33] he described a test for determining cylinder axis using Verhoeff and Lancaster-Regan dials. The manner of conducting the test is as follows, quoted directly: "Before the eye which is being tested, one places the sphero-cylinder combination already found by other methods. While the patient looks at the chart, the examiner remarks that all the radiating heavy black lines are actually of the same intensity, but when the supplemental lens (the cross cylinder) is held up before the eye the lines will probably appear unequal in intensity." Usually a 0.12 D. or a 0.25 D. cross cylinder is held in the oblique setting. He continues: "The patient usually notices a difference in the intensity of the radiating straight lines on the chart, either in both positions of the cross cylinder or at least in one of these positions. The patient is then asked to tell which position of the cross cylinder comes nearest to making the lines on the chart as a whole look uniform in intensity." Finally, ". . . when no change in the axis is necessary, the variation in intensity of the lines will be equal in both directions."

In his earlier test for power Crisp used the rotating cross chart for this purpose. The axis of astigmatism already having been ascertained, the cross of the chart is moved until one of its lines is parallel to the axis of the trial cylinder. The cross cylinder is then flipped in the principal setting. If the astigmatic trial lens is correct, each position of the cross cylinder will sharpen slightly one of the lines of the cross and blur the other. The patient decides whether the lines are alternately equally blurred and sharp.

Crisp and Stine[34] later used the rotating cross chart for a very delicate test for axis in a somewhat similar manner except that when the patient, by his answers, indicates a desire for a change in axis, the rotating cross is turned so that both its lines lie exactly astride the axis of the trial cylinder. The cross cylinder is then twirled in the oblique setting.

Using the clock face dial Wilson[35] described similar tests for axis and power of astigmatism.

While the above mentioned procedures certainly have a place in our list of tests used in refraction, I do not feel the need for them. I have tried the Crisp and Stine test many times. My chief objection is the time required to coach the

patient in the details of the test. Actually, I have found that if the patient is mentally acute, I can correct him with simpler and quicker methods—the letter charts. If he is dull the test is very apt to be too complicated for him. However, familiarity with the tests may, in selected cases, bring results. Linksz[36], in a splendid paper, points out the advantages in using the dials and the cross cylinder.

BINOCULARLY AS A POSTCYCLOPLEGIC TEST

In this test first mentioned by Sugar[37] he simply checks the axis and power of astigmatism at 20 feet and at near with both eyes open, using the cross cylinder. He points out no advantage in testing binocularly instead of monocularly. I prefer to test one eye at a time because I believe this to be more reliable.

TESTING THE AXIS FOR NEAR

Especially when a patient takes a high cylinder, and more especially for the first time, the axis of astigmatism for the reading distance should be investigated. Holding the smaller Snellen or Jaeger test types at the reading distance, the cross cylinder should be used to check the axis of astigmatism at this distance, one eye at a time. It is well known that some patients, especially those with large amounts of astigmatism, apparently require a different axis for near than for distance. Some eventually acquire two pairs of glasses, one for distance and the other for near.

THE CROSS CYLINDER WITH DUOCHROME BACKGROUND

It will be recalled that Williamson-Noble[21] in his paper on the cross cylinder pointed out that if a patient is fogged he tends to choose too great a cylinder against the rule, whereas when his hyperopia is undercorrected he tends to choose too great a cylinder with the rule. This was particularly noted when the axis of astigmatism lay approximately vertical or horizontal or within, say, 20 degrees of same.

To obviate this difficulty he uses the duochrome test several times during a refraction to keep the eye in a condition of mixed astigmatism, as mentioned previously.

In addition to this, however, he suggested the following cross cylinder test with letters on a duochrome background: "When the final correction has been obtained and the letters are equally clear on the duochrome with the glasses in the trial frame, a 0.25 D. cross cylinder is added, and it will be found that the letters on the red background are clearer when the plus cylinder is vertical, and those on the green background when it is horizontal. This is what one would expect because with both lots of letters slightly and equally blurred, the green image is in front of the retina and the red behind; that is, the eye is relatively myopic for green and therefore sees better with a plus cylinder horizontal than with it vertical. So far as the red is concerned, however, the eye is relatively hypermetropic for it and therefore prefers the plus cylinder axis vertical."

"This is not meant as a test for the amount of astigmatism present; it is only employed as a check when the patient has supposedly final correction in the trial

frame and even then need only be employed when the axis of the correcting cylinder is within 20 degrees of the vertical or horizontal meridian."

The duochrome test, in all its applications, has been very disappointing in my hands as has the above test, because too many patients cannot tell whether the green or red is sharper, even if rendered 0.50 D. myopic or hyperopic.

USING CROSS CYLINDER IN RETINOSCOPY

This method of using the cross cylinder was mentioned in an article by Crisp and Stine[34]. Shortly before Stine died he wrote me a letter describing his use of the Jackson cross cylinder with retinoscopy. I can do no better than quote his letter:

"The technique used by me in practically all cases, both with and without mydriasis and cycloplegia, is as follows:

(1) Using the plane mirror either by reflection from a distant light source, or with the self-luminous retinoscope, under-correct the least hyperopic or over-correct the most myopic meridian by at least 0.25 D. or 0.50 D., so that "with" motion is seen in all meridians.

(2) Use plus cylinders to correct the "with" moving astigmatic band.

(3) If the cylinder is of correct strength and at the correct axis, the "with" motion will be uniform in all directions of the motion of the mirror, and the central luminous reflex will be circular.

(4) (a) To check the correct placement of axis of trial cylinder, rotate the trial cylinder off-axis 5 to 10 degrees, and a new "with" moving astigmatic band (proportionately more pronounced the stronger the original astigmatic error) will be seen inclined approximately 40 degrees away from the axis of the trial cylinder. This indicates that the trial cylinder is of correct strength but should be moved toward the axis of the band.

(b) If the plus cylinder has been rotated too far in the opposite direction, a "with" moving band will appear at approximately 40 degrees to the other side.

(5) If the inclination of the "with" band is decidedly less, the trial cylinder is still at the incorrect axis, but is also too weak. If a "with" moving band is seen in the axis of the trial cylinder, the axis is correct, but the cylinder is too weak.

(6) If the new "with" moving band appears inclined more than 45 degrees from the axis of the trial cylinder, the trial cylinder is too strong and should be replaced with a weaker one at an axis a few degrees in the direction of the axis of the band. If the new "with" moving band is exactly 90 degrees from the axis of the trial cylinder, the axis is correct, but the cylinder is over-correcting.

(7) As a final check, apply the cross-cylinder (0.12 D. or 0.25 D.) astride the axis of the trial cylinder. If the axis is correct, a new band will appear moving "with" parallel with the axis of the minus component. If little or no band is seen, rotate the plus trial cylinder toward the plus axis of the cross cylinder. The action of the cross cylinder is to enhance the astigmatism when held in one position, and to reduce or neutralize it in the alternate position, and accordingly the trial cylinder should be rotated toward the corresponding axis of the cross cylinder in the position in which there is less or no appearance of astigmatism, plus toward plus, minus toward minus.

(8) Cross cylinders may also be applied parallel with the axis of the trial cylinder, once the correct axis has been determined. If the plus trial cylinder is correct, a "with" band will appear in the axis of the minus component; and an "against" band in the axis of the

plus component if one is at the point of reversal, or the spheric correction is within the dioptric limits of the cross cylinder being used."

I have used the cross cylinder in the manner described above. It is a valuable adjunct to retinoscopy.

THE CORRECTING CROSS CYLINDER

Both Smart[38] and Pascal[7] have described the simultaneous use of the correcting cross cylinder with the testing cross cylinder to determine the axis and amount of astigmatism.

A correcting cross cylinder is produced in the same manner as a testing cross cylinder. Their lenses are identical, consisting of cylinders of equal generic strength but opposite signs crossed at 90 degrees. However, the correcting cross cylinder has no long handle but is made just as any other lens in the trial case for use in the trial frame.

In testing for axis in the early stages, a testing cross cylinder twice the power of the correcting cross cylinder should be used, a 1.00 D and 0.50 D respectively. In the final stage just the opposite seems best, that is, a testing cross cylinder half the strength of the correcting cross cylinder. During the test a correcting cross cylinder of proper strength is placed in the trial frame instead of an ordinary trial case cylinder. One of its axes is placed at the approximate cylindric axis known and the test then proceeds as if a single cylinder were in the trial frame, either plus or minus, depending upon the refractionist's preference.

For power, the testing and correcting cross cylinders are similarly used, the latter lens being substituted for a trial cylinder in the trial frame and the test carried out as if it were a trial cylinder.

The reason for using the correcting cross cylinder as pointed out by Smart and by Pascal is that it keeps the eye in the condition of mixed astigmatism. Practically, its purpose is exactly the same as Williamson-Noble's duochrome test, which he uses several times during a refraction.

In the early stages of refraction I have found that it may have some merit, but in the final stages where the vision is 20/20 or better, the testing cross cylinder itself accomplishes the same purpose.

FOR MEASURING ACCOMMODATION

In this test, first described by the author, the full distance correction is worn. In front of this, a 0.25 D. or 0.50 D. correcting cross cylinder is placed with its minus axis at 90 degrees. Next, a Jaques blur-point card is held before the eye. If the patient is not presbyopic, the horizontal and vertical lines of the brack cross of the card will seem equally clear. The card is then brought slowly toward the eye until the horizontal lines appear blacker than the vertical. At this point a Prince rule is used to measure the accommodation as in other familiar tests.

If the patient is presbyopic, a + 3.0 D Sph. is added to the distance correction and the measurement taken as before, the 3.0 D. bein subtracted from the result.

What happens in the test is that the patient who is not presbyopic in this instance, looking through the Jackson cross cylinder, accommodates, thus seeing the crossed lines on the Jaques card equally blurred. Therefore, one focal line lies in front of the retina and one behind the retina.

As the card is brought closer and closer to the eye, the patient finally is unable to accommodate further and both focal lines then are forced backward. The posterior one then lies behind the retina and the anterior one lies on the retina, making the horizontal lines clearer. (If the minus cylinder is placed at 180 degrees, the vertical lines would appear clearer.)

In other tests for accommodation, I have found that it is difficult for patients to say exactly when a line or a letter first becomes blurred as it is brought nearer the eye. In the proposed test, the patient apparently can tell much more accurately when the horizontal lines, for instance, of the test card, become clearer than the vertical lines.

The chief reason for this lies in the fact that the patient has two items to compare, that is, the vertical and the horizontal lines; whereas, in the other common tests for accommodation, by the time the test object becomes a little blurred the patient has forgotten what it looked like when it was farther from the eye and perfectly clear.

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Clinical Practice

ACCOMMODATION AND REFRACTION

CONTACT LENSES IN TREATMENT OF KERATOCONUS

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The increasing recognition of the importance of contact lenses in the treatment of keratoconus has led to a quite exceptional concentration of these cases in the Contact Lens Department at the Royal Westminster branch of the Moorfields, Westminster and Central Eye Hospital. Between April, 1951, and September, 1955, more than 2000 patients were seen at the Contact Lens Department. Of these 2000 patients, 92 were sent with a diagnosis of keratoconus.

Allergy—Of these 92 cases, 15.2 per cent gave a history of allergy, including hay fever. The general rate, excluding keratoconus, for 2000 cases is 4.2 per cent, so that keratoconus patient show an incidence of allergy 3.65 times greater than the average of all cases seen in the department. These cases of allergy were distributed evenly as to age and sex.

Lenticonus—Residual astigmatism when a contact lens is worn may be presumed to be lenticular. In this series, 10 cases showed residual astigmatism exceeding 0.75 D. Both eyes were affected in 5 cases and one eye in 5 cases. Of the 15 eyes thus affected, six showed 1 D., five 2 D., three 3 D. and one 4 D. of astigmatism. It is fairly certain that many cases of symmetrical lenticonus, not revealed by this method of investigation, also exist. Lenticonus complicating keratoconus does not seem to be related to the severity of the disease.

Keratoconus Posticus—This was recorded in 6 cases.

Scrutiny of each of the 92 cases shows that almost invariably the eye with the greater total of refractive error has the worse vision and was the first eye to be affected.

There were 42 males and 50 females in this series, evenly distributed in all age groups ranging from 8 to 70 years of age. Right and left eyes were similarly affected as between males and females at all ages; the evidence does not suggest that the right or left eye is more frequently the first eye to be affected in either sex.

As a rule, the active phase of the disease is over by the time the patient has attained 27 years of age: of the cases over 27 years of age, 12.75 per cent still had 20/20 vision in one eye with spectacles. The true figure for unilateral cases is certainly higher than this, since it is to be presumed that many people having a visual acuity of 20/20 in one eye will not seek relief, or will not have been referred to the department.

In 59 cases, it was possible to record the age at which the disease first became apparent. The disease rarely begins outside the ages 10 to 25 and 67.8 per cent of all cases are first observed between the ages of 10 and 20 years, with a peak at 16.1 years. The course of the disease is not influenced by the age when it is first observed. The first eye to be affected is often in the fully-developed stage of the disease when first seen and deteriorates little subsequently. The second eye affected shows a different picture. The mean visual acuity of this group drops from 20/20 to between 20/40 and 20/60 in the first 2 or 3 years of observation. It then remains fairly steady for the rest of the 8 years as compared with the mean figure of 20/200 for the first eye affected. The curves for the second eye are parallel whether eyes having 20/20 vision with spectacles are included or excluded, and it is probable that this is indeed the course of the disease in the second eye.

On the average, the better eye already has about −1.5 D. myopia correctable to 20/20 when the case comes under observation. The distribution of refractive error at each level of visual acuity suggests that the great majority of these cases are already suffering from the disease and have deteriorated from a probable emmetropia. The disease is one of "giving way" of the central area of the cornea. In most cases this is at first regular in character and may be seen either as increasing relative myopia or increasing astigmatism or both. This may progress to as much as 4 diopters in all, but at any point irregular stretching may supervene with deterioration of visual acuity with spectacles. It is unusual for a cornea to stretch in a regular manner so as to give more than 4 diopters of total relative myopia before the stretching becomes irregular and clinical keratoconus supervenes.

The degree of astigmatism, as such, seems to have no direct relation to the visual acuity. Both spherical and astigmatic stretching may remain regular and correctable by spectacles, in exceptional cases, up to quite high figures. The presence of undoubted keratoconus in the fellow eye may be held to establish the diagnosis of keratoconus in such eyes as show these exceptional degrees of refractive error.

In any case in which deterioration of vision not correctable by spectacles is observed, it may be possible that we are dealing with an anomalous keratoconus. I have had under observation for some years a women now 52, who between 43 and 48 years of age, being a myope—10 D. with pronounced myopic fundus changes involving the macular area, suffered a progressive deterioration of vision from 20/20 to 20/60 with spectacles. Her cornea showed a slight degree of keratoconus and her vision improved to 20/20 with contact lenses. Such cases may be numerous if looked for.

In the present state of knowledge one cannot as a rule diagnose the first eye clinically until its visual acuity with spectacles begins to fall but we can diagnose the condition in the second eye very early indeed if a close watch is kept for a change of total refraction almost always towards myopia. It is here that the disease may be studied in its early active phase and here too one may hope to ascertain its etiology and apply treatment successfully. This may well mean frequent,

perhaps three monthly, refraction under a mydriatic, but in this way we may recognize the condition some 18 months earlier than is otherwise possible.

Of the 92 cases seen, only 9 were found unsuitable for contact lenses. Of the 83 cases accepted for fitting 56 have been completed and a final result obtained by September, 1955. Of these 56 cases, 34 have had their lenses more than 12 months.

Without exception, any keratoconus in which there is a red reflex should be tried out with contact lenses. Alternatively, any patient who can count fingers at one foot with spectacles should give them a trial. There is some evidence that the regular wearing of contact lenses arrests, or at least greatly reduces, the rate of progress of the disease. Perhaps even with 20/20 vision in one eye both eyes should be fitted and contact lenses worn up to the age of 30 years when the disease seems almost invariably to have burnt itself out, unless it is feasible to keep the unaffected eye under constant observation.

Allergy and a light-sensitive skin tend to reduce the wearing time and may give rise to periods when the contact lenses cannot be worn. All eyes that are not hopeless should be fitted, and in this is included extreme conus and active ulceration. However extreme the conus, it is almost always possible to fit a contact lens, albeit with much technical difficulty, and in our experience ulcerating cases have healed under a lens and the eye has become comfortable.

In no other type of case save clear but distorted penetrating corneal grafts are the visual results obtained by contact lenses so dramatic.

The effect is probably permanent in most cases. Since the contact lens abolishes the cornea optically, any increase in the cone will show only when corneal touch occurs and the lens has to be hollowed out to accommodate it. This procedure has so far been necessary in only one case in this series.

Study of the 34 people who have had their lenses more than one year is as follows: two have been lost trace, two are known to be abroad, and seven have given up—five on account of intercurrent disease or death, and two because they "can't be bothered." Year-by-year records of the remaining 23 show that all still average 13 hours of wear daily.

This question of wearing contact lenses has been dealt with at some length because there is a persistent belief that, though these patients wear their lenses reasonably well at first, they soon give them up. Our records prove that this is not true; our work is justified not only by the immediate restoration of useful sight to many young people otherwise doomed to near blindness in one or both eyes, but also by the acid test of long-term results.

Comment: This survey of a relative large number of cases of keratoconus presents little that is new as far as the general characteristics of the disease are concerned, except that there seems to be a considerably greater correlation with various types of allergy than that found in cases wearing contact lenses for conditions other than keratoconus. Whether this is cause and effect or coincidence remains to be determined.

While few actual statistics are available, it seems likely that keratoconus of low grade is much more prevalent than generally realized. One recent report, for example, showed 12 eyes, representing 6 individuals with early and minimal keratoconus, occurring in a

group of 1034 persons selected at random from several thousand during an investigation of corneal astigmatism. Most ophthalmologists agree that the active phase of the disease is usually over by age 30 and that many cases during the developmental period fail to progress to the higher degrees which are readily recognized in the course of examinations with the slit-lamp or during routine refraction procedures. It is very likely that many individuals whose best visual acuity with glasses is less than average may have a low degree of keratoconus.

From the diagnostic standpoint, considerable degrees of keratoconus present no difficulty, but the lower degrees do. In minimal keratoconus the slit lamp frequently is of no help, and the central dark shadow in retinoscopy, so familiar in the higher degrees, is not sufficiently in evidence. The patient in these early cases will, as a rule, have a lesser visual acuity than would be expected with the apparently normal condition of the media and fundi, and this should suggest a further investigation with possible keratoconus in mind.

Only one examining instrument, the ophthalmometer or keratometer, will reveal minimal keratoconus. The appearance of the mires of the instrument as reflected from the anterior corneal surface have a characteristic type of distortion which when once seen can never again be mistaken.

In this country, most eyes with keratoconus seem to see better with concave cylindrical lenses, usually of considerable strength and placed with their axes against the rule, either alone or combined with spherical elements, rather than with the spherical concave lenses suggested in this paper.

In my experience, there is no contraindication to the use of contact lenses in keratoconus when they have been properly fitted. It is imperative that the ophthalmologist assure himself of the accuracy of the scleral contact and of the corneal clearance and arrange for subsequent periodic examinations in order to detect changes in refraction or further corneal deterioration. Proper moulding and apical clearance are both essential in avoiding irritation and providing maximal vision.

Occasionally spectacles may have to be worn in addition to contact lenses by individuals who have, in addition to keratoconus, lenticonus or considerable lenticular astigmatism and there should be no hesitancy in prescribing these. Indeed supplemental spectacles are needed routinely for the presbyopic individual and these are usually prescribed in bifocal form.

Acute or chronic inflammation of the already deteriorated corneas of eyes with keratoconus, while relatively infrequent, is by no means unknown. This forms one of the hazards of the disease and it is often apparently a consequence of the wearing of improperly fitted contact lenses or of inadequate supervision of the use of even properly fitted ones. Hence the need for frequent examination by an ophthalmologist of the individual with keratoconus.

EDWIN FORBES TAIT

THE RULE OF A SUB-HARMONIC IN THE WAVE-FORM OF LIGHT FROM A FLUORESCENT LAMP IN CAUSING COMPLAINTS OF FLICKER

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Previous studies showed that the normal 100 cycle per second fluctuation of light from a fluorescent lamp is not at all likely to give rise to an appreciable number of complaints of perceptible flicker under the conditions most commonly encountered; that is, in an installation giving of the order of 10 feet lamberts luminance on the general surroundings in the visual field, with correctly operating gear and the ends of the lamp well screened. It was found, however, during the course of an earlier investigation that some fluorescent lamps showed the presence of a small 50-cycle per second fluctuation superimposed on the main 100-cycle one. The main 100-cycle per second fluctuation of the light output is, strictly speaking, the second harmonic of the main supply frequency, but in the present work it is regarded as the fundamental frequency of the light fluctuations, and the superimposed fluctuation at mains frequency is regarded as a sub-harmonic. The presence of this sub-harmonic apparently arises from a partial rectifying action in the discharge (possibly due to asymmetric emission of the electrodes), and amounts of up to 10 per cent were found in a sample of old and new lamps examined for wave-form.

An experiment using a multiple criterion technique was therefore carried out with a small number of experienced observers to determine the amount of this subharmonic required to produce perceptible flicker and various degrees of flicker discomfort at given levels of field luminance.

The experiments were carried out with "daylight" fluorescent lamps running from a 100-cycle per second A.C. supply. A rectifier was connected in series with the lamp, and the amount of rectification introduced was controlled by means of a variable resistance in parallel with the rectifier. The subject viewed a test field consisting of the end screen and the whitened side walls and ceiling of the room being used for the experiments. Fixation was not maintained, but attention was concentrated on an area between two reference marks. The lamp was mounted just above and behind the subject's head and illuminated his field of vision nearly uniformly. The subject had control of the rectifier shunt resistance, and after an allowance of two minutes for adaptation to the luminance of the field of view, he was asked to adjust the resistance control knob to produce sensations of "just perceptible flicker," "just obvious flicker," "just uncomfortable flicker," and "just intolerable flicker," in turn. During adjustment of the rectifier shunt resistance, the field luminance was kept constant. The amount of rectification

introduced at each setting was indicated by the D.C. voltage measured across the rectifier. The rectifier voltage was calibrated in terms of percentage of 50-cycle component in the light output wave-form of the lamp by direct measurement of oscillograms of this wave-form. According to the definition used, a wave-form with no 50-cycle component was given a value of 0 per cent of sub-harmonic, and a 50-cycle wave-form with no 100-cycle component was given a value of 200 per cent of sub-harmonic. The experiment was repeated at three values of average field luminance—40, 10, and 4 feet lamberts.

Although the results of the experiments showed wide variations, as might have been expected, at a field luminance of 40 feet lamberts none of the subjects required more than 4.3 per cent of the 50-cycle component on the average for flicker to become just perceptible and some required only just over 1 per cent. The average value for six subjects at this luminance level was 2.5 per cent.

The average values of percentage of 50-cycle component, P, required by each subject for the four criteria of flicker sensation have been plotted against the three values of field luminance, B, on logarithmic scales. For practical purposes of estimating the effects of sub-harmonic in a lighting installation, the points which can be properly located may be considered as falling close to a series of straight lines. These lines are roughly parallel for each criterion and indicate that a given change in 50-cycle component will produce the same change in sensation at any field luminance in the region investigated. The change in P required for the same criterion of sensation is very nearly in directly inverse proportion to the change in field luminance, or $P \sim B^{-1.25}$. To change from a sensation of just perceptible flicker to one of just obvious flicker at a given value of P requires the field luminance to be doubled. The steps between the other criteria are a little smaller, the smallest being that between just uncomfortable and just intolerable flicker which requires an increase in field luminance of 1.5 times.

When the amplitude of modulation at 50 cycles per second is plotted against average field luminance for flicker perceptibility and discomfort, a rather interesting distinction between the effect of large and small visual fields becomes evident. With the largest visual field, for a 50-cycle modulation of either a steady source or a 100-cycle fundamental wave-form, increasing the field luminance decreases the amplitude of modulation required to produce a given sensation of flicker. This means that adding a steady component or the illumination from one or more lamps with 100-cycle wave-form to the light from a lamp exhibiting a 50-cycle component will tend to increase the possibility of flicker sensation if the whole visual field is stimulated. On the other hand, in the case of a smaller visual field, increase of field luminance results in a decrease of the possibility of flicker perception or discomfort for a given amplitude of fluctuation. From this, it follows that while the addition of one correctly operating lamp alongside one exhibiting a 50 cycle component in the wave-form will not reduce the possibility of flicker perception; even in the case of illumination of the whole visual field, there is less likelihood of flicker perception when a number of small lamps are used (provided that they are not connected in series).

Preliminary tests on two small installations have shown that about 50 per cent of the tubes were exhibiting 2 per cent or more of sub-harmonic, and at least one tube in each installation exhibited over 4 per cent. The presence of these sub-harmonics, therefore, can reasonably be assumed to be sufficiently common to account for most of the genuine complaints of flicker that have arisen.

Comment: For some years, ophthalmologists have been aware of the use of flicker fusion frequency for the investigation of central and peripheral light sensitivity. Those who have been subjects in these investigations can testify as to the annoying character of a perceptible flicker from light sources, and that is the reason for the investigations summarized in this paper by Collins.

It is apparent that, at least in England, there have been many complaints regarding annoying flicker in the illumination supplied by fluorescent lamps. It would seem that 50-cycle lighting current is universally used in that country. This, of course, gives rise to a 100 per second fluctuation of light in either incandescent or fluorescent lamps, and if this were the only frequency, there would be few people indeed who would be able to observe the fluctuation, because 100 changes per second is usually far beyond the ability of the average eye to perceive. However, in all such installations, harmonics of the frequency are present. Those of higher order, of course, are still less likely to be appreciated, but those of lesser order may be.

The British investigators found that the sub-harmonic with just one-half of the cycles per second was the principal annoying factor, and they also reported some relationship between the average field luminance and the sensitivity of the subject to this particular frequency.

In the United States, there have been occasional complaints regarding flicker in lighting sources, but, in general, in areas where the electrical supply is the usual 60-cycle current with 120 fluctuations per second, complaints are uncommon.

As far as the fluorescent tubes used in this country are concerned, there is apparently less stroboscopic effect with them than with an equivalent incandescent bulb. This absence of flicker depends, of course, upon the persistence of the lighting effect during the period of fluctuation shift. In addition, practically all lamp installations are multiple with a two lamp balance thus providing a difference in the cycling of the two lamps which can be up to 180° in the cycle, but which is ordinarily about 120°. In a multiple tube installation, therefore, the illumination, although not entirely constant, is more than adequate to assure constant retinal stimulation.

In a few areas in this country, the power supply is less than 60 cycles, and in these regions there have been frequent complaints of flicker, not only with fluorescent lighting, but also with incandescent bulbs. For example, it is reported that in Buffalo, New York, which has 25-cycle current, many individuals experience annoying flicker from all lighting sources. A fluctuation of 50 per second is well within the flicker sensitivity of many of the individuals who have shared in flicker fusion experiments.

A note of caution may be interjected into a consideration of flicker, in that many individuals may be misled by a pseudo-flicker due to physical interference such as haze, or to psychologic interpretative phenomena. Included in the latter classification may be those who complain of the "cold" character of the relatively red-free fluorescent light sources, or by those who object to the greater quantity of red in incandescent bulbs. This may have some connection with the high-point of visual acuity in relation to spectrum position, as exemplified by so-called deuteranopic and protonopic individuals.

EDWIN FORBES TAIT

THE LENS

ON THE SO-CALLED SENILE EXFOLIATION OF THE ANTERIOR LENS CAPSULE: A CLINICAL AND ANATOMICAL STUDY

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The condition described as "senile exfoliation of the anterior lens capsule" presents a clinical picture comprising a characteristic formation, giving the appearance of an exudate, on the anterior surface of the lens, and the appearance of light grey particles (flakes or dandruff) in various positions in the anterior eye. In this study the pathological entity will be described as "exfoliation" or the "exfoliation syndrome" and the term "material of exfoliation" will be used to designate the actual substance of the abnormal formations in the exfoliation syndrome.

Two different theories have been advanced to explain the nature of the material of exfoliation:

(1) Material of exfoliation is a deposit on the anterior surface of the lens as well as in other positions in the anterior eye, as maintained by Malling and Busacca. According to Busacca the deposit both on the surface of the lens and elsewhere presents a characteristic histologic picture, that of the so-called "deposits of Busacca."

(2) Exfoliation originates as a degenerative condition of the lens capsule, as maintained by Kraupa and Vogt; and the material of exfoliation appearing elsewhere in the eye is material rubbed away from the degenerated capsule and carried by the intraocular fluid to various positions in the anterior eye. Vogt and his pupils claim to have found characteristic abnormalities in histologic preparations which lend support to this theory.

The purpose of the present study on exfoliation has been especially to try to determine which of these two conflicting theories is correct or at least the more probable. The clinical observations are based on exhaustive examinations of patients with exfoliation, partly at the University Eye Department at Rikshospital and at the University Eye Department at Ullevål Sykehus, and partly in the author's private practice. For the examinations a Haag-Streit slit-lamp, fitted with a corneal microscope with magnifications of 9½ ×, 19 ×, 20 ×, and 40 ×, and a Goldmann's gonioscope, were used; on a few occasions a Zeiss slit-lamp was also used. In describing the pathologic formations on the anterior surface of the lens, three areas are distinguished: the central disc, the peripheral band, and the clear intermediate zones separating the two affected areas. The peripheral

band and the central disc differ considerably in clinical appearance. The peripheral band and the bridges connecting it with the central disc have a most characteristic granular appearance, and are of a grayish white color which causes them to stand out clearly against the background of the clinically normal lens capsule. The central disc, on the other hand, is homogeneous and is not differentiated by its texture from the lens capsule itself. There does not seem to be any criterion for the perception of the central disc itself other than the difference of color between it and the clear zones that surround it. By comparison with these intermediate zones, it presents a more or less pronounced grayish color. The peripheral band with its bridges and the central disc are so totally different in clinical appearance that it seems reasonable to suppose that they also differ anatomically. The central disc may be altogether absent in cases of exfoliation, but the peripheral band is always present. This suggests the possibility that the appearance of the granular material of which the peripheral band and the bridges are composed is the essential feature of exfoliation and that the material forming the central disc may well be of quite a different character. So far as its clinical appearance is concerned, the granular material may in some cases be seen as a continuous circular girdle on the lens surface behind the iris, apparently forming a deposit on the surface of the lens capsule. On dilation of the pupil, parts of this granular deposit may be torn off, and clear intermediate zones will then appear. The remaining granular material then has the configuration of the peripheral band and the bridges. Close proximity of or contact between the posterior surface of the iris and the anterior surface of the lens seems to be a necessary condition for the formation of this material on the lens.

Gonioscopic examinations of a series of patients with glaucoma simplex showed the presence of flakes in the angle of the chamber in 6 of the 32 eyes with exfoliation. All the flakes were in the lower angle on the trabeculum or on the root of the iris.

Anatomic and histologic studies were also made of 23 eyes with exfoliation enucleated because of glaucoma absolutum dolorosum following glaucoma simplex. The gross anatomic findings show beyond reasonable doubt that the granular material of exfoliation on the anterior surface of the lens (the peripheral band and bridges) forms a deposit on the surface of the lens capsule. The technique employed did not reveal any pathologic substance corresponding to the central disc. Intermediate clear zones were produced experimentally in enucleated eyes by rubbing away the granular material on the surface of the lens with a piece of the iris. From the histologic studies, it appears that the so-called "deposits of Busacca" represent the granular material of exfoliation which may be observed on the lens, and the material of exfoliation observed as flakes in the anterior eye. No abnormal material was observed on the surface of the lens in the position of the central disc. Degenerative changes in the lens capsule of the kind that Vogt and his pupils regarded as characteristic in exfoliation were not found in any of the eyes with exfoliation examined histologically. The lens capsule itself has the same histologic appearance in eyes with exfoliation as in those without exfoliation. Besides the so-called "deposits of Busacca," other deposits of an

uncharacteristic form were observed in many eyes. These other deposits occur in eyes from younger as well as from older patients, and may occur whether the patient has exfoliation or not. With the routine staining methods these two types of deposits are both colored a faint pink and can be distinguished only by their form. With Mallory's stain, however, the deposits of Busacca are generally colored blue, while the atypical deposits are a reddish-yellow.

Although the present study does not provide any basis for drawing conclusions as to the nature of the central disc, certain possibilities may be considered:

(1) The primary formation on the anterior surface of the lens may consist of a deposition of granular material of exfoliation in the position behind the iris. In this case, the appearance of this deposit on the lens capsule might result in discoloration of the capsule in the position of the central disc.

(2) The so-called deposits of Busacca may be precipitated from the intraocular fluid. In this case, it is possible that a precipitate of a similar kind may be formed in the position of the central disc, appearing clinically as a homogeneous grayish film.

(3) Finally, it may be that when "deposits of Busacca" come away from the surface of the lens, a thin layer of material actually belonging to the superficial layer of the lens capsule is removed together with the deposit, so that the entity perceived clinically as the central disc really consists of the residual disc-shaped remnants of this superficial layer of the capsule.

Although it cannot be stated that genuine material of exfoliation does not appear in the angle of the chamber, the evidence suggests that even if it does, it is not the cause of the so-called glaucoma capsulare; on the contrary, it seems that exfoliation and glaucoma simplex share a common causative factor, so that they often occur simultaneously. As a rule the exfoliation will appear before the manifest glaucoma, but it may appear later; consequently, glaucoma simplex, with or without exfoliation must still be considered a primary glaucoma.

On review, the histologic findings of Vogt and his pupils do not provide an adequate basis for the contention that exfoliation originates as a degenerative condition of the lens capsule. It is still an open question, however, whether the histologic abnormalities found by them are artefacts or whether they do in fact represent some pathologic condition of the lens capsule.

Comment: This most interesting monograph focuses our attention on a clinical entity which is not rare but is frequently overlooked. The incidence varies considerably, and this is not due to the interest of the examiner or necessarily to the thoroughness of the examination since Thomassen found the condition in 80 per cent of patients with glaucoma simplex in Norway and in only 0.5 per cent of a similar series in England.

Dvorak-Theobald (Tr. Am. Ophth. Soc. 1953, *51:* 385) arrived at the same conclusions as Sunde; that what is called exfoliation of the lens capsule is really a pseudo-exfoliation. The flakes or dandruff seen on the lens capsule are deposits or accretions of an unknown substance. True exfoliation is seldom seen and, when it is, it is due to exposure to intense heat over a prolonged period of time, e.g., puddlers in a rolling mill.

There is no question that patients with pseudo-exfoliation are frequently seen in glaucoma clinics. The deposition of accretions in the angle and trabeculum is frequently

considered as a factor in producing the rise in intraocular pressure. The reviewer has operated on several patients with exfoliation without increased pressure. Unfortunately, no suitable follow-up to determine whether they eventually developed glaucoma is available.

The author examined 23 eyes with exfoliation which were enucleated for absolute glaucoma, and this forms the basis of the histologic findings. There is little doubt that exfoliation is frequently seen *in vitro* and *in vivo* in glaucomatous eyes. The question yet to be answered is: What effect does removal of the lens play in the course of the glaucoma? It has been proved histologically that the condition is really a deposit of accretions, giving rise to a pseudo-exfoliation. Such being the case, one might expect to find such accretions to continue to develop on the hyaloid following intracapsular cataract extraction.

Kirby, in discussing Irvine's paper (Arch. Ophth., 1940 *23*, 138) states, "The incidence of glaucoma in 50 per cent or more of cases does not prove that the exfoliation causes the glaucoma but that the two are associated. The only logical procedure in these cases is a filtering operation. I should not consider the removal of a relatively clear crystalline lens from an eye with useful vision to be justified on the basis of the control of the glaucoma." This dictum is still sound, though the reviewer feels that one might be justified in removing such a lens a little earlier than one might if no evidence of exfoliation was present.

Further clinical studies on the fate of eyes having lens extractions with pseudo-exfoliation would be of great value.

P. Robb McDonald

FAILURE IN CONGENITAL CATARACT SURGERY: A STUDY OF FIFTY-SIX ENUCLEATED EYES

THE 1955 JACKSON MEMORIAL LECTURE

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Tr. Am. Acad. Ophth., 1956, *60:* 345–367

The prognosis for the surgical treatment of congenital cataract is not so good as that for the surgical treatment of cataracts in the adult. A certain percentage of the failures can be attributed to congenital anomalies that interfere with the restoration of vision; others are the result of well-recognized early and late postoperative complications. Clinical observation suggests that certain of these complications may be associated with the type of operative procedure employed. Histopathologic evidence establishing such an association has been sought in 56 eyes removed after surgical failure.

The operations employed for the correction of congenital cataracts are (1) simple discission, usually repeated a number of times; (2) through-and-through

discission (Ziegler operation); (3) discission followed by linear extraction; (4) simple linear extraction; and (5) linear extraction with limbal incision and iridectomy, with or without sutures. Optical iridectomy is used so rarely that it is not considered in this discussion.

The most frequent complications of congenital cataract surgery are glaucoma, pupillary displacement or occlusion, and retinal detachment. Seen less often are corneal changes (e.g., edema and bullous keratitis), epithelization of the anterior chamber, uveitis, sympathetic ophthalmia, atrophy of the globe, phthisis bulbi, endophthamitis, and panophthalmitis. Glaucoma as an operative complication of congenital cataract may be caused by (1) a rapid swelling of the lens which pushes the iris forward and blocks the pupil; (2) retention of a large amount of cortex in the anterior chamber; (3) blocking of the pupil as a result of iris bombée; (4) formation of peripheral anterior synechias as a result of delayed restoration of the anterior chamber; and (5) blocking of the pupil by vitreous and filling of the anterior chamber by vitreous.

The principal causes of pupillary displacement have been given as prolapse of the iris, contusion of the iris, and prolapse of the vitreous. In one series it was found that the greater the number of operations, the higher the percentage of pupillary displacement. Occlusion of the pupil may result from the formation of a thick membrane composed of capsule and lens material, or of a complicated membrane due to inflammation, organized exudate, or hemorrhage. It is often difficult to differentiate between proliferation of the capsule and the formation of an inflammatory pupillary membrane. Discission with de Wecker scissors should be used in operating upon these membranes or aftercataracts so as to prevent pulling on the ciliary body, which might cause hemorrhage in the anterior chamber. Another factor in the production of occlusion of the pupil may be failure to perform an iridectomy in cases in which the pupil will not dilate preoperatively. It has also been pointed out that as long as there is cortical material in the area of the discission, injury to the posterior capsule (vitreous) breaks up resorption and is one of the causes of inflammatory pupillary membrane formation. Still another cause of membrane formation in the pupillary area which may occlude the pupil or produce posterior synechias is the discontinuance of mydriatics before all the cortex is absorbed.

Retinal detachment is an important postoperative complication, which, in the opinion of many authors, is most apt to appear after a long period of delay. The average interval between discission and the onset of detachment has been said to be 24.6 years. A number of reasons for the delay have been advanced, but it is generally agreed that the more the vitreous is disturbed, the greater the danger that retinal detachment will develop. Late detachment has been found much more frequently after needling than after linear extraction. Progressive myopia, too, must be considered as a possible etiologic factor. Corneal edema, bullous keratitis, and vascularization of the cornea sometimes develop in patients undergoing congenital cataract surgery as a result of other severe complications. Velhagen, for instance, suggested the possibility that corneal dystrophy might occur if vitreous touched the posterior surface of the cornea after vitreous loss

or after a breaking of the hyaloid which would permit vitreous to enter the anterior chamber.

Phthisis bulbi was found by Huerkamp in 69 per cent of the eyes that developed severe complications postoperatively. Interestingly enough, the usually harmless iridectomy for prolapsed iris has been found to be a dangerous procedure, creating a predisposition to phthisis bulbi, when performed in the first year of a child's life.

Clinical experience suggests a definite relationship between the type of operation and the quality of the results obtained. Some form of linear extraction seems to be the operation of choice. If the pupil can be dilated easily preoperatively, the simple linear extraction is probably best; if the pupil is difficult to dilate, iridectomy followed by linear extraction is indicated. No one operation, however, can be recommended to the exclusion of all others. In cases of membranous cataract, shrunken cataract, or aftercataract, linear extraction is quite obviously not indicated because of the danger of vitreous loss when an attempt is made to grasp the capsule. Some form of discission, with the least possible damage to the vitreous, is then indicated.

The procedures preceding enucleation in this series were needling (40, or 71.6 per cent), linear extraction (14, or 25 per cent), and operations of unknown type (2, or 3.4 per cent). Of the eyes in which needling had been done, 29 (72 per cent) had had multiple needlings; 11 (25 per cent) had had a single needling (one of these had had a Ziegler through-and-through operation. One of the linear extractions followed a needling. Glaucoma was present in 26 (46 per cent) of the 56 eyes; and in 75 per cent of these it followed one or more needlings. Uveitis, intraocular hemorrhage, the formation of cyclitic membrane, and vitreous block were contributing factors. The frequency with which anterior peripheral synechias were observed seems to emphasize the importance of early restoration of the chamber and to substantiate the clinical observation that the injection of air at the end of the operation is indicated, especially when the anterior chamber has been opened.

Detachment of the retina occurred in 23 (41 per cent) of the cases in this series. Pupillary membrane formation was present in 12 cases, in most of which the pupillary space was small. This suggests the advisability of doing a full iridectomy whenever the pupil cannot be widely dilated before surgery.

Late detachment of the retina developed on an average of 22.2 years after the last needling in 37.9 per cent of the eyes subjected to multiple needlings. Multiple needlings, therefore, seem to be the least desirable of all the procedures. Although the series is small, late retinal detachments after linear extraction were significantly fewer, statistically, than after multiple needlings.

Comment: This reviewer was fortunate to hear Dr. Cordes' masterful presentation of the Jackson Memorial lecture. This timely article should focus every ophthalmologist's attention on the seriousness of congenital cataracts. Because of associated congenital abnormalities and the age of the patient, the prognosis is not nearly as good as it is in patients with senile cataracts. Many eyes are undoubtedly lost because of injudicious surgery. Having read this article, every ophthalmic surgeon should look up Dr. Cordes'

paper on "Surgery of Congenital Cataracts," Am. J. Ophth., 1948, *31:* 1073. Though the article suggests that linear extraction as a primary procedure results in fewer complications than the repeated discission operation, any ophthalmologist who has tried both procedures will undoubtedly agree with the suggested conclusions. It is very questionable whether any patient who can get around or who has 20/50 or better vision, should have surgery for congenital cataracts. Should surgery be decided upon, the child should be well anesthetized, preferably with endotracheal anesthesia. The pupil should be maximally dilated with subconjunctival injections of Neo-Synephrine and atropine, if necessary. The keratome incision can be intracorneal at the limbus above and it is well to place a chromic suture through the edges of the corneal incision. A knife-needle tract should be made below for the injection of air. The anterior capsule should be removed with a cystitome or back-tooth capsule forceps. This is followed by slow and patient irrigation of lens material out of the anterior chamber. A surprisingly large amount of lens material can be irrigated free if one is not hurried. At the conclusion of the operation, the corneal suture can be tied, air may be injected into the anterior chamber, and if the pupil is not fully dilated, another subconjunctival injection of Neo-Synephrine and atropine may be necessary. This method of surgery frequently obviates the need of a discission of the posterior capsule. Should this be necessary, usually one discission suffices. Congenital cataract surgery is not for the novice or the occasional surgeon. These patients with a life expectancy of many years, should be given every opportunity for obtaining a successful result.

P. Robb McDonald

THE CORNEA

FUNGUS KERATITIS: A REPORT OF THREE CASES

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A.M.A. Arch. Ophth., 1956, *56:* 257–264

The widespread use of cortisone and antibiotics has been accompanied by an alarming increase in fungus infections in various organ systems, such as the respiratory and gastrointestinal tracts. Occasional cases of mycotic keratitis have been reported in the literature since 1879, but whereas they formerly averaged little more than one case a year, in the one year 1955 six new cases were described. The authors' purpose, therefore, is (1) to report three new cases of corneal ulcer in which fungi were demonstrated in the enucleated specimens; (2) to restate the necessity for etiologic diagnosis, both clinical and pathologic; and (3) to consider the part played by the use of cortisone and antibiotics in the pathogenesis of mycotic keratitis.

The recent report by Mitsui and Hanabusa (Brit. J. Ophth. 1955, *39:* 244) of four cases of fungus keratitis following topical corticosteroid therapy for various other ocular conditions led the authors to look with suspicion at an eye enucleated for an uncontrolled hypopyon ulcer in which there was a long history of corticosteroid therapy. The pyroxylin (Celloidin) sections of this specimen stained with routine hematoxylin and eosin showed an acute pyogenic inflammatory process in the anterior segment. Further sections, however, stained with periodic acid-Schiff (McMannus) technique, showed a gross infestation with a fungus which was tentatively identified from its morphologic characteristics as one of the aspergilli. After this discovery, all new specimens received in the ophthalmic pathology laboratory with a clinical diagnosis of any ocular infection were stained with periodic acid-fuchsin as well as with routine hematoxylin and eosin. In addition, specimens received in the preceding months were reviewed. Two more cases were found as a result, making a total of three eyes with mycotic keratitis, all of which had been enucleated in a period of a little more than a year.

All three cases had several features in common. All occurred in farmers—an occupational coincidence noted by many previous authors. All the patients had sustained trivial corneal injuries with vegetable matter. All were treated for varying periods with corticosteroids and antibiotics. In none had the diagnosis of mycotic infection been made before enucleation or, for that matter, before the use of the special staining technique. It must be stated that when the hematoxylin-and-eosin-stained sections were minutely examined in retrospect, a few

* The $250 prize for the best paper presented at the June 1956 meeting of the Section on Ophthalmology, A.M.A., was awarded to the authors of this paper.

ghosts of mycelia could occasionally be seen; nevertheless, the vast bulk of the organisms remained hidden and were overlooked on routine examination. As long ago as 1913, the value of differential stains in demonstrating the causative organism in an ocular disease was clearly established, and this point therefore need not be given further consideration.

Hervouet and Lenoin, in reporting two cases of aspergillosis of the cornea, pointed out the fact that this fungus keratitis presents most frequently as a common hypopyon ulcer and is usually not recognized as a fungus infection. Their experience showed conclusively that both the pathologist and the clinician must be constantly on the lookout for fungi in every case of hypopyon ulcer.

The presence of gross mycelia in the surface exudates in two of the present specimens indicates that it would be easy to obtain a smear and a culture of the organisms from a scraping of such ulcers. The role of the fungus in these cases is hard to determine, since there are three possibilities: (1) The fungus may be the primary pathogen or essential etiologic agent; (2) it may act as a secondary invader in a bacterial or viral infection, altering the course of the disease; or (3) it may be present only as a saprophyte. Although the part originally played by the fungus in these three cases cannot now be ascertained, the massive invasion of the cornea and the extension of the hyphae into the anterior chamber suggests that it was active in the end-stage of the disease process seen in the pathology laboratory.

The essential problem posed by these cases is whether or not the use of antibiotics and corticosteroids altered the clinical course in such a way as to allow the initial lesion to become seriously infected by the fungus. In the first place, it is possible that the growth of the fungus itself may be modified by therapy, and in the second it is possible that normally saprophytic or symbiotic fungi may become facultative pathogens as a result of alterations in host resistance produced by corticosteroid therapy. In addition, preliminary animal experiments, which are to be published by one of the authors (A.P.L.), have shown that both topical corticosteroids and certain antibiotics may facilitate the development of some corneal fungus infections.

Although much experimental work is needed to clarify the effect of corticosteroids and antibiotics on fungus lesions of the cornea, clinical experience to date indicates that the application of corticosteroids to corneal lesions involves the risk of facilitating mycotic, bacterial, or viral infections. In particular, corticosteroid and antibiotic therapy seem to be hazardous when there is an epithelial defect or any active infection in the cornea.

Comment: An increase in number of reported cases of keratomycosis could mean that more cases are occurring, that more cases are being diagnosed, or that more are being reported. If more cases are actually occurring, these must result from either an increase in the number of eye injuries in farmers, which is unlikely, or to facilitation of infection by steroids or antibiotics in cases where fungus contamination of the cornea has accidentally occurred. Ley has demonstrated potentiation by cortisone and oxytetracycline of experimental fungus keratitis in animals.

It is unfortunate that primary treatment with antibiotics, steroids and non-specific

medications apparently was instituted by the referring physician in each of these cases, without an attempt being made to obtain an etiologic diagnosis by scraping or culture of the corneal ulcer.

A refreshing contrast is provided by a case recently treated by Liebman and Mangiaracine at the Massachusetts Eye and Ear Infirmary, to be reported by them. Scrapings of a corneal lesion, resulting from hay injury, were found on routine Gram stain to contain fungus spores. Hyphae were demonstrated with methylene blue. Cultures were taken on Sabouraud's medium. A special suspension of Mycostatin was prepared and the patient was placed on topical instillation plus systemic dosage. Cultures revealed aspergilli. The patient made a slow recovery and currently has 20/70 vision with a pinhole.

The authors present convincing evidence of the value of Schiff-periodic acid stain in demonstrating fungi in pathologic sections. It is to be hoped that their report will reduce the necessity for such sections by directing attention to the means of making the diagnosis *in vivo*.

HENRY F. ALLEN

THE INTRAOCULAR PRESSURE

INDICATIONS FOR AND RESULTS OF PERIPHERAL IRIDECTOMY IN ANGLE-CLOSURE GLAUCOMA

SAMUEL T. ADAMS

Tr. Canad. Ophth. Soc., 1954–1955, 7: 227–237

Peripheral iridectomy is now recognized as an important step in the management of angle-closure (narrow-angle) glaucoma. The information for this study, in which the selection of cases for this operation is discussed and its results are analyzed, was drawn from 56 cases of angle-closure glaucoma; 39 of the eyes were subjected to peripheral iridectomy. There is good clinical evidence that in any eye the pressure in the posterior chamber is higher than that in the anterior chamber. In the eye predisposed to acute angle-closure glaucoma, this increase in posterior chamber pressure pushes the lens-iris diaphragm forward, causing the iris root to come into apposition with the anterior chamber apparatus, the trabeculum, thus blocking the outflow of aqueous and causing an acute rise in intraocular pressure. The principle of peripheral iridectomy in angle-closure glaucoma is to establish an alternative passage other than the pupil by which aqueous can flow from the posterior to the anterior chamber. With these pressures equalized, physiologic iris bombé is prevented and the iris root is not pushed against the trabeculum. If the trabeculum is free during a phase of elevated tension, it must be assumed that the impediment to aqueous outflow is in or beyond the trabeculum, and peripheral iridectomy will therefore do no good.

Hence the procedure is theoretically of no use in open-angle glaucoma. If the iris is permanently adherent to the trabeculum (peripheral anterior synechiae) throughout all or most of its circumference, peripheral iridectomy, though it will decrease the iris bombé, will not be able to reduce the synechiae, and hence the aqueous outflow will still be impeded. The acute attack will not occur again, but chronic elevation of tension will persist.

In accordance with these principles, this form of operation was carried out in four types of eyes:

(1) Acute angle-closure glaucoma—tension not normalized.

(2) Acute angle-closure glaucoma—tension normalized.

(3) Fellow eye of eye with acute angle-closure glaucoma—with some record of tension elevation and with no record of tension elevation.

(4) Sub-acute angle-closure glaucoma.

The rationale for recommending peripheral iridectomy in these various types of glaucoma was as follows:

Type 1. There is no question but that eyes with acute glaucoma with high tension not normalized by medication within an arbitrary period must be operated on. The decision as to whether the trabeculum will be normal enough to resume useful function if the iris reverts to its normal relationships must be made on the basis of the history of previous attacks, duration of present symptoms, and duration of tension elevation, together with the gonioscopic appearance.

Type 2. If the tension is normalized rapidly with medical treatment (or with no treatment) and the eye becomes quiet and good vision is restored, both doctor and patient are often loath to undertake surgical treatment. Nevertheless, these eyes should have a peripheral iridectomy to prevent further glaucoma from occurring. In this survey, of 21 eyes normalized from an acute attack and not operated on, 8 had a further acute attack within from two days to three years. In five of the remaining 13 eyes, the lack of a further acute attack could be explained, leaving 8 that were free from glaucoma.

Type 3. The incidence of acute angle-closure glaucoma in fellow eyes is high enough to make prophylactic peripheral iridectomy advisable. The very nature of acute angle-closure glaucoma is reflected in rapid rises and falls in tension; therefore, on the basis of the tension measurements obtained in this study, the percentage of fellow eyes in which elevated tensions develop may safely be assumed to be higher than 54.1 per cent. Some of the measurements that were normal may merely have been obtained during a normal phase.

Type 4. The decision for operation in cases of subacute angle-closure glaucoma is usually more difficult for both patient and doctor. If the history is suggestive and elevations of tension are recorded in one eye, the presence of narrow angles and bulging irises is usually enough to warrant peripheral iridectomy in both eyes.

A small peripheral iridectomy is relatively easy to do and has a minimum of possible complications. It preserves the optical, cosmetic, and physiologic normality of the eye. In all but five of these cases, the technique described by

Chandler and Barkan was used. The main points in this technique are the *ab externo* incision, the firm resuturing of the wound, and the re-formation of the anterior chamber by air injection. A miotic drug was used before and after all operations, and on the following day a short-acting mydriatic. Alternately on successive days the pupils were constricted and dilated to prevent formation of posterior synechiae. There was no higher incidence of postoperative peripheral anterior synechiae after the five operations that were performed by keratome incision and closure of the wound by conjunctival sutures only, but the risk seems an unnecessary one.

The longest follow-up is about 3 years and the shortest about 3 months (average 1½ years). Of the 39 eyes subjected to iridectomy 33, or about 85 per cent, have had normal tension without medication since operation. Three more are normal with medication. Three have tensions averaging in the middle 30's in spite of medication. Almost all the angles have less iris bulge than before operation, and 36 have posterior trabeculum showing in at least half of the circumference of the angle.

Serious complications occurred after three operations. One patient had sympathetic ophthalmia and two had severe intraocular hemorrhage, occurring after the first postoperative day. One of these patients also had a cataract, presumably as a result of lens traumatization during the operation. Nonserious complications consisted of iris prolapse (4 cases), posterior synechiae (3 cases), peripheral synechiae (1 case), a flat anterior chamber the day after operation which eventually reformed permanently (1 case), and absence of peripheral iridectomy as a result of failure to remove enough iris tissue (2 cases). In one of these last eyes, the tension became elevated again and a second operation was performed; the other has shown no elevation of tension, presumably because the pupil is distorted and this prevents pupillary block.

Comment: This is an excellent evaluation of the indications for peripheral iridectomy which is much-needed by the ophthalmologist who, wishing to use this relatively new procedure, finds that its nonselective use is often followed by failure. The important fact in the use of peripheral iridectomy is the knowledge that two things are necessary to permit normalization of tension in angle-closure glaucoma: (1) re-establishment of flow from the posterior to the anterior chamber, and (2) reopening of the trabecular spaces which have been blocked by iris. Peripheral iridectomy may be successful in acute angle-closure glaucoma in which the tension could not be normalized before operation. Only 5 eyes were of this type. In a larger series of this type of glaucoma not normalized before operation, it would probably be found that cases of failure to open enough of the blocked angle and, consequently, failure to normalize tension would be more frequent. Gonioscopy, if it can be done, may be helpful here.

In eyes normalized before operation and in the fellow eye with or without record of previous tension elevation, peripheral iridectomy is ideal but even here one may occasionally observe failure due, in the case of the acute glaucomatous eye normalized before operation, to postoperative synechias where there is borderline angle block at the time of operation. In the fellow eyes one may experience difficulty if the edges of the iridectomy are caught in the wound or if only the anterior layer of the iris is removed.

In the subacute angle-closure cases, peripheral iridectomy should be done only if the

gonioscopic findings indicate that enough of the angle is open. If long-standing synechias are present and they cover most of the angle circumference, iridencleisis would probably be a wiser procedure.

One could argue the advisability of using a miotic or mydriatic drug immediately postoperatively. Adams uses a miotic. Others advocate such drugs as atropine.

The discussion of the complications in this paper is excellent.

H. Saul Sugar

NEUROLOGY

TENSION HEADACHE

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Am. J. M. Sc. 1956, *232:* 105–111

Tension headache is undoubtedly the most common variety of headache as well as the most common complaint of patients in the office practice of general medicine. It occurs in relation to constant or periodic emotional conflict which may be conscious or unconscious. Tension headaches have no prodromata, are usually bilateral, occipital, or frontal, and may be accompanied by anxiety and such symptoms as nausea and vomiting, dizziness, weakness, irritability, and constipation. The frequency and duration are variable, but an attack may last for weeks. The discomfort has been described as constant and boring, unlike the throbbing quality of migraine headache; bizarre, rarely interfering with sleep; a tight feeling, as a band around the head; vague and dull; or a sensation of pressure in the head; a dull aching tenseness in the neck; the head caught in a vise, or scalp on too tight, or "top of my head blowing off." The headache tends to be worse at night. The pain begins in the occipital zone, extends into the forehead and may center there or in the vertex. They are poorly defined, with a complete lack of any features characterizing them as another type of headache.

OTHER COMMON HEADACHES

Conversion (Hysterical) Headaches

These headaches are often almost indistinguishable clinically from tension headaches. The main distinction is that in conversion headaches the symptoms represent a specific unconscious symbolic meaning and the conversion mechanisms are prevalent. Wolff (*Headache and Other Head Pain*, New York, Oxford University Press, 1948) states that these patients "use the word pain to describe sensations resulting from the effects of non-noxious stimulation because past

conditioning experiences have modified their interpellation of any head sensation. . . . Distortions of judgment in such persons may be shown in the misevaluation not only of the pain threshold but also of the intensity of head pain. Furthermore, these persons may show defects in other sensory discrimination, should these happen to involve symbols significant to the given individual."

Migraine Headaches

The following comparison of the characteristics of 1000 cases of migraine and a similar number of cases of tension headache is worthy of quotation (Neurology, 1954, *4:* 773):

	Per cent	
	Migraine	Tension
"Family history of headache	65	40
Age of onset		
less than 20 years	55	30
over 20 years	45	70
Prodroma	60	10
Frequency		
constant or daily	3	50
less than 1/week	60	15
Duration		
constant or daily	0	20
1–3 days	35	10
Type throbbing	80	30
Location		
unilateral	80	10
bilateral	20	90
Associated symptoms, vomiting	50	10

Migraine and tension headaches did not differ in respect to incidence, sex, precipitating occurrence, mood change, onset and termination."

Histamine Cephalgia

This is a unilateral vascular headache which usually begins in the later decades of life. It begins and ends suddenly and generally lasts less than an hour. It tends to awaken the patient at night one or two hours after he has gone to sleep, and the severity of the pain makes the patient get out of bed and pace the floor. At its height the pain is associated with watering and congestion of the eye, rhinorrhea or stuffiness of the nostril, sweating and often visible dilation of the temporal vessels of the involved side of the head.

PHYSIOLOGY. In tension headaches a muscular or vascular mechanism may act independently or concomitantly. The tense, apprehensive, or anxious patient seems to be constantly poised to go into action. The persistent tension causes a sustained contraction of the skeletal muscles of the head and neck, with resulting pain.

PSYCHOLOGIC CAUSES. In most cases of tension headache the precipitating

psychic factors are largely unconscious. However, many patients are aware of the associated anxiety. Environmental demands of an intellectual, physical, social or economic nature beyond the capacity of the patient's personality may also produce headache.

TREATMENT OF TENSION HEADACHES

Psychotherapy. The most important single factor in the psychotherapeutic process is the emotional relationship between the patient and the physician. The aeration and ventilation of wholly or partly unconscious emotional conflicts to sincerely interested and sympathetic physician may be helpful. A simple explanation of the effects of emotion on bodily function may be beneficial. Reassurance, suggestion and re-education are other techniques which may help the patient to gain the necessary security and readjustment to life.

Environmental manipulation. This procedure consists in helping the patient to so alter stressful situations in his work, recreation, family or social life that he will not exceed his emotional capacity. A sustained hobby may be beneficial in securing relief from the stresses of daily living.

Pharmacotherapy. The efficiency of medication does not depend entirely on its pharmacologic action. The importance of dosage, timing and mode of administration cannot be overstressed. Strong suggestion from a respected physician as to the therapeutic benefits to be expected from any particular drug is notoriously effective in the therapy of tension headaches. The following drugs are valuable adjuncts to the psychotherapeutic treatment of tension headaches.

(1) Acetylsalicylic acid or Bufferin in doses of 0.3 to 0.6 gm. (5 to 10 gr.) and repeated in one or two hours will often give symptomatic relief and make psychotherapy easier.

(2) Fiorinal (Sandoz) is one of the best sedative-analgesic preparations for the temporary relief of tension headache. Each tablet consists of 0.05 gm. (¾ gr.) of isobutylallylbarbituric acid, 0.13 gm. (3 gr.) of acetophenetidin, 0.2 gm. (3 gr.) of acetylsalicylic acid, and 0.04 gm. (⅔ gr.) of caffeine. When taken in dosage of one or two tablets every four hours, Fiorinal tends to prevent a mounting build-up of nervous tension and, in addition, seems to relax the musculature about the head and neck. Since it has a barbiturate component it is contraindicated for prolonged use and should be restricted in general to the early stages of psychotherapy, to infrequent tension headaches in stable individuals, or to those patients resistant to psychotherapy.

(3) Miltown (Wallace) and Equanil (Wyeth) are identical tranquilizers often effective in the treatment of mild and moderate tension headaches. Either drug may be administered to adults in an initial dose of 400 mg. (one tablet) three or four times daily. When symptoms are reduced the dosage may be halved as is necessary if the patient complains of drowsiness.

(4) Precerpine in oral doses of 0.25 to 0.75 mg. daily may at times reduce or abolish tension headache. Depression may result in susceptible individuals and several days may be required for reduction in tension.

(5) Thorazine (Smith, Kline & French), or chlorpromazine may reduce or

abolish tension headaches within a few days following its initial administration. It is administered to adults initially in a dose of 10 mg. after each meal and is gradually increased to a total of 100 mg. daily over a period of a week.

(6) Octin and Valoctin (Bilhuber-Knoll) contain methyliso-octenylamine and are often effective in ordinary tension headaches as well as those with a vascular component.

(7) Ergotamine preparations are primarily indicated in "pure" vascular headaches such as migraine, but are also useful in "impure" combinations of muscle spasm and vascular headaches which are not completely responsive to the usual therapy for tension headaches. Contraindications to their use include peripheral vascular disease, coronary heart disease, hypertension, impaired renal or hepatic function, pregnancy, sepsis, toxemia, and malnutrition.

Comment: Since headache is a major complaint of many patients visiting the ophthalmologist, this article is of interest. There is no question that the majority of cases will have underlying stress situations—in fact, many individuals will volunteer such information if questioned sympathetically. Whether such a clear-cut distinction between migraine and tension headache can be made in usual office practice is questionable, since stress situations and basic personality traits can be a part of either picture. For example, Ryan in his textbook, *Headache*, denotes the patient with tension headache to be of the perfectionist personality type who is unable to adapt himself to his environment and reacts to such stress by headache. On the other hand, it is stated by other authors that the individual with migraine is insecure, and reacts by becoming inflexible, over-conscientious, meticulous, and perfectionistic. The resultant frustrations in daily life lead to the migraine attack.

Because much of value in treating these patients lies in the field of education, the physician must be able and willing to take adequate time to explain the mechanisms and to help the individual to reorganize his environmental situation. I believe that this can best be done in severe cases by a trained psychotherapist. Certainly the wisdom of indiscriminate prescription of the newer drugs such as meprobamate (Miltown; Equanil), and the Thorazine series by the ophthalmologist is questionable—both because of the potential side-effects, and because also the basic psychic mechanisms should be uncovered, rather than "tranquillized," for lasting relief.

Other effects of emotional stress are most evident to the ophthalmologist who is looking for such relationships. Central serous retinopathy is an example in certain cases. The recurrences of iridocyclitis can often be related to periods of exceptional stress and fatigue. These factors should be kept in mind by all of us who are caught in the headlong pace of modern living.

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A CASE OF SYPHILITIC PERINEURITIS OF THE OPTIC NERVE

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Ophthalmologica, 1956, *131:* 290–293

Syphilitic perineuritis of the optic nerve was never frequent and has now become comparatively rare, especially in Switzerland where the incidence of syphilis is constantly declining. Particular interest, therefore, attaches to a case discovered in a 33-year-old man referred to the Ophthalmological Clinic of Berne. He had first consulted an ophthalmologist a few months before on account of headache. Hypermetropic astigmatism was found and glasses were prescribed. The headache was temporarily relieved but returned about two months later, accompanied by muscae volitantes in the left eye. Thereupon, he consulted a different ophthalmologist and was at once referred to the clinic with a diagnosis of bilateral papillary edema, vitreous hemorrhage, and suspected blood disorder or cerebral tumor. In addition to the ocular complaints, the history taken on admission showed loss of hair and chronic bronchitis. At first sight, the ophthalmoscopic picture might have been taken for one of papillary stasis, but the presence of a slight fibrinous exudate in front of the papillae and a few precipitates on the posterior membrane of the vitreous seemed to point to edema of an inflammatory nature. Lumbar puncture showed that the intraspinal pressure was normal, but serological tests produced a strongly positive Bordet-Wassermann reaction in the blood, although in the cerebrospinal fluid the same reaction was negative. The diagnosis of syphilis thus established explained the symptoms of headache, hair loss, and chronic bronchitis, and showed that the involvement of the optic nerve without alteration in visual function was due to syphilitic perineuritis. Further questioning revealed the fact that the primary chancre had appeared a year and a half before.

Treatment was entrusted to the Dermatological Clinic, and the patient's ocular status was re-examined at intervals. Now, after six specific cures, the results of the Wassermann test are negative, the papillary edema has disappeared completely, and the papillary borders are clearly defined. The corrected visual acuity remains at its original figure of 1.5 on both sides.

Since a cure can almost always be secured if antisyphilitic treatment is started in time, histopathologic studies of this condition are not available. Uhthoff and Igersheimer, however, came to the conclusion that syphilitic perineuritis is a complication of a basal syphilitic meningitis in which the initial involvement of the optic nerve sheaths takes the form of a thickening of the pia mater caused by lymphocytic and plasmocytic infiltration. The severity of the ocular condition depends on the extent to which the infiltration progresses, ranging from simple papillary edema without visual impairment to total involvement of the optic nerve with loss of visual acuity and possibly postneuritic atrophy of the nerve. The pathogenesis suggested explains why the condition, which usually appears in the late secondary stage of syphilis, is almost always bilateral.

Since the incidence of optic nerve involvement in patients with syphilis has been set at no more than from 4 to 9 per cent in general, it is easy to understand why its occurrence in Switzerland is exceptional.

Comment: The moral of this paper is that despite the decreasing incidence of syphilis, it is still occasionally with us. Certainly a blood serological examination should be a first consideration in any patient with optic nerve involvement. There is a tendency to do fewer Kahn or Wassermann tests in routine examinations which is to be deplored.

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EXTERNAL DISEASE

MEIBOMIAN GLAND TUMORS

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Meibomian gland tumors may be either benign or malignant. Generally speaking, the benign tumors are diagnosed only infrequently; consequently, the age and sex distribution have not been determined. They may attain considerable size and assume the form of a hard lobulated mass in the tarsal portion of the lid. Treatment by surgical excision is advisable, although recurrences are frequent if the excision is not complete.

Malignant Meibomian tumors have been noted more frequently, and in 1950 the total of meibomian carcinomas in the world literature was 97. Other cases have since been reported, but no exact enumeration of the reported cases can be made because of differences in terminology, the diverse criteria for diagnosis, and incomplete breakdown of the reported material. These tumors occur in both sexes with almost equal frequency according to some authors, though others have stated that women are more often affected. The tumors usually develop in middle life, but cases have been reported in children.

The clinical picture of meibomian carcinoma is focussed about the growth of a painless firm nodule that develops more frequently in the upper than in the lower eyelid. Multiple Meibomian carcinomas have been reported in a single lid, and the malignant potentiality of these tumors is demonstrated both by extension and by metastasis. Metastasis usually takes place along the path of lymphatic drainage. Significantly, regional node involvement may be detected

at the time the primary tumor is diagnosed or it may be discerned clinically at a later date.

The treatment of Meibomian carcinomas has, in general, paralleled the treatment devised for other neoplasms of the skin and its appendages. Surgical attack on the eyelid tumor has been the most frequent mode of therapy. Many cases have shown that incising, curetting, cauterizing, or incompletely excising these tumors will be followed by recurrence, often with growth at an apparently accelerated rate. Consequently, wide excision of the primary lid tumor is the preferred treatment, with closure by simple approximation of the incised edges or plastic reconstruction. Radiation therapy for Meibomian carcinoma employing radium application and the implantation of radium seeds has been generally unsuccessful. The experience with x-ray therapy has been decidedly more promising, although no five-year cure has been reported.

Material obtained from the pathology collection of the Institute of Ophthalmology, supplemented by specimens from the Armed Forces Institute of Pathology, has been studied for the purpose of establishing a classification of Meibomian gland tumors, determining histologic criteria for their diagnosis, and correlating their histologic and clinical features.

The Meibomain glands develop as an ectodermal ingrowth from the inner parts of the fused lid margins during the fourth month (80 mm. stage) of intrauterine life. They form a single row of parallel vertically arranged glandular structures occupying the tarsal plate of both the upper and the lower lids. Their number has been set at 25 in the upper lid and 20 in the lower, though some authorities believe there are more. The linear central tube or duct of each gland is lined with stratified squamous epithelium, while the secretory alveoli, or acini, consist of a basement membrane separating the supportive elements from a single layer of small flat undifferentiated cells. Centrally in the acinus are the larger, more mature cells which are polyhedral in form and contain many fat droplets. The lipid content of these cells is responsible for the characteristic yellow color associated with the meibomian glands and is disclosed by special fat stains or demonstrated by the coarse vacuoles left in the tissue specimen after fat dissolution. Culmination of the secretory process occurs when the nuclei of the large central cells degenerate and the cells break down—a holocrine type of secretion—to release a mixture of cell remnants, fat, fatty acids, and cholesterol. Replacement of the secretory cells is accomplished to some extent by mitosis of cells in the periphery of the acinus but principally by mitosis of duct cells located near the mouth of the acinus. The duct cells then become incorporated in the secretory alveolus and undergo the characteristic maturation of sebaceous elements.

Tumors may be considered to have originated from the Meibomian glands when (1) they arise in the sharply demarcated tarsal portion of the lid and show either direct continuity with a Meibomian gland or conspicuous proximity between gland and tumor; and (2) there is a histologic resemblance between the cells of the normal gland and the aberrant cells of the tumor. On the basis of these criteria, 21 cases of Meibomian gland tumor were assembled, 19 of which

are reported for the first time in this study. Classification based on the general organization and cytologic characteristics of the tumor showed that 5 were benign (1 hyperplasia, 3 adenoma, 1 hamartoma) and 16 were malignant carcinomas. Both the acinar and the duct portions of the gland participate in the tumor growth, and there is no evidence to suggest that specific tumors arise from the duct as opposed to the acini.

The benign tumors began insidiously with the painless development of a mass in the tarsal portion of the lid and increased gradually in size, usually producing thickening and distortion of the lid. Hyperemia and ulceration of the overlying skin and conjunctiva occurred, although ulceration was relatively late in developing. Treatment in each case consisted of excision. From all indications, the only sequel to be expected after resection of a benign tumor is local recurrence if the excision is incomplete.

The malignant Meibomian gland tumors, usually called adenocarcinomas, are here termed carcinomas because this designation is equally descriptive, simpler, and more applicable to malignant tumors showing no trace of glandular organization. The morphologic changes and metastasizing potentialities found in these tumors constitute indisputable proof of their malignancy. Prominent features in their histologic diagnosis are the general organization of the tumor cells into masses, the characteristics of the individual cells, and the relations between the tumor and the adjacent structures.

The histologic characteristics of the individual tumor cells are of prime importance in establishing the diagnosis of Meibomian carcinomas. Carcinoma is indicated by the loss of orderly cell differentiation and evidence of excessive mitotic activity. Mitosis is only rarely seen in the normal gland; it is occasionally present in the benign tumors, but in all carcinomas large numbers of dividing cells may be seen, indicating rapid growth.

Indications are that even the malignant Meibomian tumors grow in an expansile fashion without any predilection for invading normal tissue. The presure of the expanding tumor causes the orbicularis and the anterior lid structures to bow forward, forming a pseudocapsule for the tumor.

One metastatic lesion was encountered in this series. Treatment consisted of simultaneous excision of the primary tumor and the metastatic lesion, which had developed in a preauricular lymph node, followed by radiotherapy. Adequate surgical excision of the primary neoplasm in the lid is the treatment of choice. Excision of the full lid thickness is favored because infiltration may occur and resection of the full lid thickness does not appreciably impair the cosmetic result. The presence of metastatic lesions is an indication for radiotherapy. Whether or not enlarged regional nodes are present at the time of the operation on the lid, the patient should be followed for at least five years. Local recurrence of the lid tumor and the late appearance of metastases are always possible. Prophylactic excision of regional and cervical lymph nodes is not advocated, because prompt and vigorous therapy directed against the metastatic lesion has been shown to be capable of controlling the disease. Not a single recurrence or extension of meibomian carcinoma is known to have followed definitive surgical treatment.

Follow-up of these patients has been far from complete, but the fact that several have survived without recurrence for more than five years shows conclusively that this type of carcinoma can be successfully combated.

Comment: The present study and analysis of Meibomian gland tumors focuses attention on the important characteristics of these lesions. The higher incidence of Meibomian carcinomas in the upper lid is due to the relatively greater number of glands in the upper than in the lower lids. In a total of 21 Meibomian tumors in this study, 16 were malignant, and in all of these a high degree of mitosis was present. Growth generally occurred in an expansile fashion, with little prediliction for invasion of normal tissue. Ulceration of the lid-margin and conjunctival surface occurred in some cases, but the subjective symptoms were mild in all. Metastases to the regional nodes were common.

The failure of radiation therapy as an initial procedure in the Meibomian malignancies is worthy of emphasis, and is of startling revelation in view of the common practice among radiotherapists of treating these lesions by radiotherapy as a primary procedure. The author advises primary excision of the lesion, and of the involved regional lymph nodes when metastases are present, followed by radiation. However, in the absence of metastases, prophylactic excision of regional and cervical lymph nodes is not advocated.

The importance of differentiating Meibomian carcinomata from basal cell tumors is pointed out because of the infrequency of metastases in the latter.

HUGH L. ORMSBY

THE OCULAR MUSCLES

CONTRIBUTION TO PARTIAL TENOTOMY

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Between 1952 and 1954, 42 partial tenotomies were performed on the internal rectus in patients with convergent strabismus. In 27 patients, orthophoria was practically obtained by the operation. Follow-up examinations one or two years after the operation revealed permanence of the satisfactory result in most of the patients operated on. The average reduction of the angle of the squint by partial tenotomy was 6 degrees. Nine patients were surgical failures. An excessive effect in the sense of limiting the abduction or of postoperative development of a divergent strabismus was never observed.

Partial tenotomy also was performed on the external rectus. Unilateral partial tenotomy was performed in 8 patients, and bilateral partial tenotomy also was performed in 8 patients. In 3 patients partial tenotomy was combined with myectomy or reinsertion. Two patients with exophoria were considerably improved with regard to the positive range of the fusion after the operation; in one patient it was improved from +5 to +45, and in the other patient from zero to +20. The reduction of the angle of the squint in divergent concomitant strabismus was about 12 degrees per operation, but convergence exercises contributed considerably to the satisfactory result of the operation. In three patients, orthophoria which has not been present preoperatively occurred in the presence of binocular fixation. In some patients a divergence in elevation of the eyes was observed postoperatively which has not been demonstrated previously. The unequalness of the muscle incisions, or a not uniform exposure of the muscle may have been responsible for this defective operative result. The author, however, considers the results obtained satisfactory, and he intends to use partial tenotomy even more frequently in the future particularly in patients with concomitant alternating internal squint, with squint angles below 12 degree and abduction plus. Partial tenotomy may be a very useful operation for strabismus, providing the intervention is carried out correctly and with appropriate after-treatment.

PHYSIOPATHOLOGY AND DIAGNOSIS OF CONCOMITANT STRABISMUS

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Concomitant strabismus may be defined as "a syndrome characterized by a certain deviation of the visual axes and by a disturbance of binocular vision." This definition is somewhat vague but it will serve as a basis on which to discuss the treatment of concomitant strabismus in relation to its physiopathologic groundwork. First, it shows that there are two elements to be considered in the cure of strabismus: (1) disappearance of the deviation; and (2) normalization of the binocular vision. A cure that is merely esthetic, though sometimes all that can be accomplished, should only be accepted as a last resort. Second, it serves as an outline for the discussion of (1) the sensory element in strabismus; (2) its motor element; (3) certain special features in connection with it; and (4) its differential diagnosis.

Before taking up the sensory element in strabismus, we must recall certain points relating to normal binocular vision. The most important of these is that with two eyes we see one image. The mechanism by which the fusion is accomplished is unknown, but the components of binocular vision are well established.

(1) Each retinal point has a visual line of its own which corresponds to the visual line of a certain other point in the opposite retina. The outstanding example of these corresponding or paired retinal points is provided by the foveas in normal binocular vision. Now, if the two images of an object fall on corresponding points, the object will be seen as one. If two points receive the images of two different objects, the objects will be seen in superposition, and the result will be confusion. If on the other hand the two images of a single object fall on noncorresponding points, the object will be seen double, unless the disparity of the points is low enough to produce stereoscopic vision.

(2) The images sent to the brain by each eye must be sufficiently alike or they will not be fused. This means that the visual acuity should be almost the same in both eyes.

(3) The neuromuscular motor apparatus must also play its part by bringing the image of the fixed object to the foveas. Finally, an important point to be considered is the development of binocular vision, which takes place rather slowly. Normal binocular vision is an acquired function. This can easily be understood when it is remembered that the foveas are scarcely developed before the fourth month, that convergence hardly exists before the sixth month, that accommodation is achieved about the second or third year, and that normal visual acuity is attained only at about three or four years. Binocular vision is thought to be established at about the same age, but it remains highly labile until the age of five or six. The early appearance of abnormal conditions, e.g.,

deviation of the visual axes, will lead to anomalies in the development of binocular vision (abnormal retinal correspondence, amblyopia) which become increasingly difficult to correct the longer the treatment is delayed. Normal retinal correspondence is probably an inborn phenomenon that may become disturbed in pathologic conditions.

Disturbances of binocular vision constitute the sensory element in strabismus. Diplopia, which ought to follow the lack of parallelism in the visual axes, is not always found in children with strabismus, although it may occur at the beginning in certain cases of late strabismus. When it does, however, it never lasts more than a few days because one of two mechanisms operates to overcome it. Neutralization, the first of these, is negative; abnormal retinal correspondence, the second, is positive. The mechanism of neutralization (or suppression) is unknown, but the fact itself is commonplace; only when our attention is engaged by an object will that object be perceived by the brain. Neutralization is a binocular phenomenon. The visual field of the deviated eye, taken alone, is perfectly normal. Neutralization or suppression becomes so intense in many cases of monocular strabismus that it persists even when the governing eye is covered, and then it becomes compulsory suppression or amblyopia.

Amblyopia may be divided into four types according to the manner of fixation: (1) foveal fixation, (2) true excentric or extrafoveal fixation, which is very frequent, (3) wavering fixation, seen only in very young children, and (4) a complete lack of fixation, which rarely occurs in strabismus without organic lesions or nystagmus. This division of amblyopia into types has great practical importance because, while occlusion of the good eye may prove effective in the treatment of foveal fixation, it is contraindicated in the extrafoveal type.

Abnormal retinal correspondence is essentially an active process of adaptation to the new conditions created by the deviation of the visual axes. Whatever the mechanism by which it is achieved, the binocular vision so obtained is never normal. Consequently, in treating strabismus, false retinal correspondence should always be normalized.

The motor element in strabismus, which is essential to its appearance, is very diverse, including anatomic anomalies at rest, dyssynergy of accommodation and convergence, and various forms of paresis. More than one of these factors will usually be found in each case.

Special features requiring consideration in patients with strabismus are the importance of preserving convergence (since there can be no good binocular vision without good convergence): (1) the neuropsychiatric state of the children with strabismus; and (2) acute concomitant strabismus in the adult, which is usually due to trauma and which can easily be remedied by a slight surgical correction.

The differential diagnosis concerns chiefly ocular paralysis, the retraction syndrome, and various forms of pseudostrabismus which arise in children who are orthophoric by the screen test and whose binocular vision is normal but who have been treated for strabismus because of such factors as interpupillary distance that is either too large or too small, epicanthus, an overwide nasal bridge,

or an alpha angle that is either too large or too small. Of these, only pseudostrabismus has any real practical importance.

THE RETINA AND VITREOUS

STUDY OF REBOUND PULSATION IN THE RETINAL ARTERIES AND ITS CLINICAL VALUE

CONTRIBUTION TO THE DIFFERENTIAL DIAGNOSIS OF PAPILLARY STASIS

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The use of Gullstrand's ophthalmoscope in studying the rebound pulsation of the retinal arteries provides more precise information about this phenomenon than that to be found in earlier observations. Briefly described, it consists of a rapid displacement of the artery, especially at its bends, during systole, followed by a slower return to the original position during diastole. It is a physiologic phenomenon that may be observed in all healthy subjects with normal eye grounds. It is more distinct in the young and is but little influenced by the general arterial pressure. It is seen especially in the retina; in the papilla, though visible, it is less clear. Occasionally pulsation of the retinal reflections, always in synchrony with the pulse of the radial artery, is its only manifestation.

In order to determine the factors influencing rebound pulsation, the author studied 88 patients with eye-ground changes. Weakening or cessation of the pulsation was found in patients with (1) narrowing of the retinal arteries (especially in retinitis pigmentosa); (2) atrophy of the optic nerve, even when narrowing of the arteries was absent; (3) embolism of the central retinal artery; and (4) papilledema of intracranial origin from the very beginning to the advanced stages. In cases of choroiditis and retinal periphlebitis, on the other hand, as well as in those of inflammatory capillitis and retrobulbar neuritis, the rebound pulsation was easily discernible; in patients with pseudoneuritis it was always very distinct.

The absence of the rebound pulsation found in all patients with papillary stasis can apparently be used as an additional help in the differential diagnosis of edema of intraocular origin beginning in the retrobulbar sector of the optic nerve and the edema produced by an inflammation or by toxins acting on the nerve fibers of the edge of the papilla. In the latter case, there is no narrowing of the reflux channels of the liquid in the sheaths of the optic nerve, or of the venous

blood. The pulsation is therefore usually visible. Absence of the pulsation may corroborate the differential diagnosis in the initial stages of papillary edema, in particular; it is especially useful in hypermetropic children, who often present a pseudoedema of the papilla. A distinct rebound pulsation in such cases seems to exclude a diagnosis of intracranial edema. Further studies will be needed to confirm the diagnostic value of this method of studying papilledema—a method which has nothing in common either theoretically or practically with the ophthalmodynamometric methods of Bailliart and of Sobanski.

Various hydrodynamic, physiologic, and animal experiments carried out by the author tend to confirm his findings on the rebound pulsation of the retinal arteries, and to establish its clinical and diagnostic value.

Comment: The author appears to have added a valuable differential diagnostic sign to the meager symptomatology of early papilledema. The difficulty of this differential diagnosis in an occasional case makes one welcome any significant addition to the diagnostic armamentarium.

Observation of the rebound or serpentine pulsation of the retinal arteries is, however, not easy. Its degree varies from an accentuated displacement of the vessel of more than its width to a mere locomotion of the arterial light reflex or of the reflexes from the inner surface of the overlying retina. Since the differential diagnostic value of this finding lies not in the degree of the pulsation but in its presence or absence, it is proportionate to the skill of the observer in noting the faintest locomotion. The author observed the return of the rebound pulsation in one instance after removal of a brain tumor, while a considerable degree of papilledema still existed, and in another case of increased intracranial pressure associated with a blood dyscrasia, when, after a few months of therapy, the general condition improved.

The scope of clinical usefulness of this observation is not entirely known and further studies should be made in a variety of fundus lesions.

BERTHA A. KLIEN

CHANGES IN THE OCULAR FUNDUS IN BLOOD DISEASES

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M. Clin. North America, 1956, *40:* 1209–1216

Many hematologic diseases produce characteristic changes in the fundus of the eye and the observation and interpretation of these changes provide important information about the patient and his illness. These changes, which are often referred to in a general way as retinopathy, consist of changes in color of the fundus or of its vessels, hemorrhages, exudates, and, at times, edema of the optic disks. With such a limited number of changes, it is often impossible to

make a specific diagnosis of the type of blood dyscrasia, but there are certain recognized and fairly definite findings that often point the way to the correct diagnosis.

In most patients, the pupils must be dilated if the eyegrounds are to be examined properly. One drop of a 1 per cent solution of paredrine (hydroxyamphetamine hydrobromide) in each eye usually provides satisfactory dilatation in from 20 to 30 minutes. This drug has very little cycloplegic effect and most patients experience little if any blurring of vision. The effect is of short duration and the patient is often unaware of any change in his vision.

Anemia from any cause may produce retinal changes. The fundus loses its brilliant reddish reflex and takes on a paler, more yellowish hue. The retinal vessels also lose their distinguishing color and the arteries and veins approach one another more closely in color. Retinal hemorrhages usually appear when the concentration of hemoglobin reaches 35 per cent or 5 gm. per 100 cc. of blood. The fact that these hemorrhages appear cannot easily be explained, but they are probably dependent on increased capillary permeability. This permeability is thought to be due to anoxemia or other toxic factors. Retinal hemorrhages do seem to appear earlier and in greater numbers in patients who are anemic from such causes as malignant disease with hemorrhage.

Small exudates, called toxic or toxic anemic exudates to distinguish them from the cottonwool exudates of hypertension, may also be found. These lesions and those of hypertension, which are otherwise identical, can usually be told apart because the hypertensive exudates are accompanied by other changes, such as narrowing and sclerosis of the arterioles.

Loss of vision does not occur in these patients and the retinopathy is asymptomatic unless hemorrhage involves the macula, a rather rare occurrence in anemia alone. Loss of vision and even blindness may develop in a patient whose anemia is the result of sudden and repeated hemorrhages, but in this case the loss of vision is probably due to more than the anemia alone.

In patients with polycythemia, the fundus takes on a darker color, hence the name cyanosis retinae. Either primary or secondary polycythemia may produce this change and there is nothing to differentiate the two on examination of the fundus. According to Elwyn, changes in the fundus begin to appear when the red cell count reaches 8,000,000 or the concentration of hemoglobin reaches 115 per cent. In most cases, however, the appearance of the fundus would excite suspicion even before these levels were reached. In addition to the color change in the fundus, the vessels, especially the veins, become large and engorged and are often nicked in a sausage-like manner by a crossing artery. Hemorrhages may occur but are not common.

Papilledema may occur in polycythemia, probably as a result of the plugging of the smaller vessels around the optic nerve head. It must also be remembered that papilledema often results from hemangiomatous tumors of the posterior fossa, which may also produce polycythemia. The triad of polycythemia, papilledema, and tumor of the posterior fossa may present a difficult diagnostic problem, but it should always be kept in mind and patients in whom it appears

should always be suspected of having such a tumor. Not until the possibility of its presence has been ruled out can the papilledema be assumed to be due to polycythemia alone.

Retinal hemorrhages often occur in all types of leukemia, but are more frequent in acute cases than in chronic ones. They are also found more frequently in myelogenous leukemia than in lymphatic leukemia. They may appear early in the disease before any other hemorrhagic phenomena have been detected. The characteristic lesion is the white-centered hemorrhage, though not all the hemorrhages will have this characteristic white center, which probably represents an actual conglomeration of leukocytes surrounded by blood. The appearance of these lesions often enables the observer to diagnose the systemic illness correctly as leukemia.

Papilledema may also occur; in fact, it appears more frequently in association with leukemia than with other blood disorders. The mechanism for the production of papilledema in leukemia is not understood, but there may be leukemic infiltration and thrombosis of small vessels about the optic nerve head. Leukemic infiltration along the retinal vessels and into the choroid is an uncommon finding, but it may occur in patients with extremely high leukocyte counts. The retinal infiltrates appear most often as white lines along the peripheral retinal veins; at times, they are accompanied by hemorrhagic extravasations as well.

Purpuric hemorrhages occur in the eye just as they do elsewhere in the body. The appearance is the same whether the hemorrhages are due to essential thrombocytopenia or to thrombocytopenia from other causes such as aplastic anemia or leukemia. An interesting finding in cases of thrombotic thrombocytopenic purpura is the occurrence of small white exudates in the absence of any hemorrhagic findings. This is the only lesion of the fundus reported in the relatively few cases of this disease in the literature. Its occurrence is not surprising because cottonwool patches are relieved to represent small ischemic infarcts of the retina. In this particular disease, hyaline thrombi plug the vessels and when this occurs in the retina, the result is the small cottonwool patch.

Changes consisting of retinal and vitreous hemorrhages have been reported as occurring in the fundi of nine Negroes suffering from sickle cell anemia.

The retinopathy of lupus erythematosus consists of rather numerous soft exudates grouped around the posterior pole of the eye, that is, near the optic disc. Exudates may appear in any of the collagen diseases, but in lupus erythematosus they are distinguished by this characteristic location, the reason for which is unknown. Occasionally, the exudates are found in a similar distribution in dermatomyositis, but patients in whom this distribution is found should certainly be given an L.E. clot test.

Finally, a number of patients have been seen at the Mayo Clinic in recent years with papilledema of undetermined origin subsequently thought to be due to infectious mononucleosis. Because of the lack of other neurologic signs and symptoms, such patients are often given a diagnosis of pseudotumor cerebri and may be subjected to air studies in a search for intracranial lesions before the true nature of their trouble is discovered. Infectious mononucleosis should,

therefore, be kept in mind as a possible, though not well recognized, cause of papilledema in obscure cases.

Comment: This is an excellent resumé of the ophthalmoscopic findings in diseases of the blood and should perhaps be read in the unabridged original version.

A blood dyscrasia, not included by the author, which may cause puzzling retinal hemorrhages is Waldenstrom's macroglobulinemia. This disease is characterized by pathologic high molecular globulin bodies in the serum, due probably to dysfunction of the reticulo-histiocytes.

While the milder form of the disease merely leads to purpura of the skin and does not usually produce fundus changes, there is a severe form with disturbances of the central nervous system, subfebrile temperatures, severe anemia, swelling of the lymph nodes, splenomegaly, and marked retinal hemorrhagic diathesis.

BERTHA A. KLIEN

SYSTEMIC DISEASE

VESSELS OF THE OCULAR FUNDUS AS A GUIDE TO PROGNOSIS

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Brit. M. J., 1956, *1:* 1501–1507

Certain changes in the vessels of an ocular fundus are significant only so far as that particular eye is concerned. Other changes can foreshadow similar disease in the second eye without permitting special conclusions about the rest of the body. Most important, however, are the retinal vascular phenomena that throw light upon the condition of other organs and systems. Taking these three categories in order, Coats's disease may be considered as an example of the first, Eales's disease of the second, and arteriosclerotic retinopathy of the third.

In interpreting fundus signs, it must be remembered first that the vessels of the retina nourish only its anterior percipient cells. The choroidal vessels nourish the posterior half, and indeed all the percipient layers at and immediately around the fovea centralis. Second, the opthalmoscopic picture is often modified by erratic proliferation of the retinal pigment cells and the adjacent layer of the choroid (Bruch's membrane) as a result of trauma, neoplasm, degeneration, or inflammation. Third, the vessels may vary widely within normal limits. Direct ophthalmoscopy provides a simple method of inspecting the vessels of the retina magnified about 15 times. The ophthalmoscopic findings, however, must always be carefully correlated with the clinical history and with the results of other meth-

ods of examination. The ophthalmologist cannot afford to ignore a patient's medical background, and he must keep in mind that disturbed vision is often the first symptom of systemic disease. Patients with hypertensive disease, diabetes, or maladies of the blood-forming organs, to mention only a few, may all present themselves for eye tests without having had a medical examination recently.

Besides the vessels, other features of the fundus picture require mention. Most vascular abnormalities are not pathognomonic of one particular condition, so that other signs—for example, exudates, pigmentary degeneration, or localized atrophy—will often provide etiologic clues. Examination of a fundus should follow a systematic plan, starting at the optic disk, proceeding towards the periphery of each quadrant along the course of the main retinal vessels, and finally embracing the macula lutea. Although it is common to speak of the retinal arteries, structurally and functionally these vessels fall into the category of arterioles. To what extent their state indicates that of the rest of the arterial tree is not precisely known, but it is at least certain that retinal arteriosclerosis is often associated with sclerosis of other arteries, and particularly of these supplying the brain. The behavior of the choroidal arteries, on the other hand, commonly differs from that of other parts of the arterial tree. Premature choroidal sclerosis sometimes besets otherwise healthy young people, and a retina ravaged by ischemia may therefore occasionally be seen, even though the ophthalmoscope reveals no abnormality in the retinal vessels themselves.

Coats's disease, which is characterized by massive retinal hemorrhage with exudation, usually attacks a healthy boy with no signs of disease in the other eye. At first the affected eye may show nothing worse than a few small hemorrhages and exudates; but sooner or later huge plaques of coagulation necrosis splashed with blood are seen. Venous and arterial distention follow and ultimately the retina may be pulled from its bed by organized connective-tissue strands growing forward into the vitreous. Although the state of the fundus vessels prognosticates destruction of the affected eye, the outlook for the other eye is good.

Eales's disease, like many other ocular maladies of unknown origin, has often been labelled tuberculous, but evidence to incriminate the tubercle bacillus as its cause has not been found. Sudden blurring of vision in one eye is the characteristic mode of onset. Rapid clearing of the initial hemorrhage is the rule, but in spite of remissions and even intermissions, purposeless multiplication of the retinal vessels eventually spreads until the whole fundus is involved. Not until some new wonder-drug has been found to control the as yet unidentified agent which brings such havoc to the retinal blood vessels will Eales's disease cease to threaten the sight of its victims.

The ophthalmoscopic signs of hypertensive disease have been described by numerous clinicians, and inevitably identical phenomena have been interpreted differently. The vascular changes seen are (1) tortuosity of the arteries; (2) intensification of the arterial light streak; (3) indentation of veins where crossed by arteries; (4) angular deviation of a vein where crossed by an artery; (5) forward thrusting of a vein where it crosses in front of a sclerosed artery; (6)

obscuration of veins where arteries cross in front of them; (7) "silver-wire" arteries; (8) narrowing of arterial caliber; (9) irregularity of arterial caliber; (10) arterial sheathing; (11) microaneurysms; and (12) engorgement of veins. It is hardly feasible to place these 12 vascular changes in order of severity. They have to be considered collectively, interpreted in relation to other fundus abnormality, and correlated with the rest of the clinical facts. If one of them were to be singled out as the most important, it should probably be the ninth. Sudden intense narrowing of the arterial caliber repeatedly discernible across the fundus is an important danger signal and has been commonly supposed to mean spasm. The question of the part played by arterial spasm in producing fundus change is most complicated and many problems still remain to be solved, but it is probably true, as Pickering says, that spasm has been too freely adduced as a reason for changes that can more logically be explained by organic vascular stenosis.

Small dark retinal aneurysms are the earliest sign of diabetic retinopathy, but months or even years may elapse before the patient notices any disturbance of vision. Many aspects of diabetic retinopathy remain a mystery, but it now seems clear that duration of disease is the most important factor in its production. Fundus changes are evident in most patients after 15 years, and it is exceptional for any to remain unaffected at the end of 20 years. The ultimate prognosis for vision is poor once even the earliest changes of diabetic retinopathy have become visible.

Long-continued hypertension and renal insufficiency are viciously interrelated, and the fundus picture is greatly modified by the speed of the systemic changes. The quicker the constitutional degeneration, the more rapidly, as a rule, will the retinal arteries become stenosed. Edema is then prominent, with swelling of the discs, cotton wool patches and snow-bank exudates of the retina, and possibly exudative retinal detachment in both eyes.

Characteristic changes in the fundus vessels may also be seen in patients with obstruction of the central retinal vessels, retinal angiomatosis, and various hematopoietic and vascular diseases. The prognostic implications of these and other retinal vascular phenomena are not always self-evident. Prognosis, however, is one of the physician's most important duties, and although complete certainty is seldom attainable, careful marshalling of the available evidence will at least permit an approximate forecast.

Comment: A critical evaluation of this subject is a difficult enterprise and the author has done justice to his subject in most parts. His division of ocular vascular disease into three groups, *viz.*, purely local alterations, lesions of importance in relation to the fellow eye, and changes with systemic implications, may be put to good practical use, especially by the novice.

His discussion of the ocular findings in hypertensive disease suffers, as most articles on this subject, from a confusing terminology. He does a disservice to the mutual understandings between internist and ophthalmologist by discussing, for example, the manifestations of hypertensive retinopathy under the term of arteriosclerotic retinopathy.

Any discusser of hypertensive fundi should make it his prime task to emphasize the necessity for a careful and separate evaluation of purely hypertensive phenomena on the

one hand and of organic (sclerotic) lesions on the other hand in interpreting these findings for prognosis. While both categories of vascular signs are frequently combined in all variations of degree on both sides, we also have those fundi which exhibit almost exclusively either hypertensive or arteriolar-sclerotic changes. The distribution of the latter implies the presence or absence of systemic hypertension, while the former are always an indication of a systemic disease.

Purely hypertensive findings such as edema of optic nerve and retina, cotton wool patches, and focal spastic contractions are completely reversible if they occur in fundi with mild or no organic vascular changes. Developing in fundi with advanced arteriolar disease they have a much more adverse prognostic significance and may indicate, for instance, a malignant phase in a long standing essential hypertension or the end stages of a chronic glomerulo-nephritis.

Many hypertensive fundi never develop edema of optic nerve and retina or ischemic infarcts (cotton wool patches) but may show an extensive retinopathy of the arteriosclerotic type, consisting of small, brilliant white lipoid deposits, hemorrhages and exudates. The constituents of this retinopathy do not differ from those of an incidental circumscribed arteriosclerotic retinopathy except by their greater extent, being complications of a more diffuse (hypertensive) arteriolar sclerosis. These fundi, which belong to patients with essential hypertension of long duration, may also develop thromboembolic (nonspastic) occlusive vascular disease, and the edema incidental to these events must be differentiated from the hypertensive type.

BERTHA A. KLIEN

THE VISUAL PROGNOSIS IN DIABETES MELLITUS

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Acta ophth. 1956, *34:* 201–207

The practical importance of the visual prognosis in diabetes is considerable. The increase of cases with longstanding diabetes means an increase of cases with severe disabling retinopathy. Workers having a pessimistic view of the visual prognosis in diabetes often quote Dolger (Proc. Am. Diabetes A. 1946, *6:* 396) who reported 200 cases of diabetes with an age of onset at less than 50 years. Of these, 13.5 per cent became blind or almost blind.

The present study deals with 1205 cases of diabetes. The visual acuity has been considered in relation to sex, age of onset, and duration of diabetes. Patients who had received medication other than insulin which was supposed to influence the cause of vascular disease were not included in the study.

Study of the visual acuity indicated a decrease in vision with duration but on the whole the decrease was moderate. The visual prognosis was worse in the higher age-of-onset groups and definitely worse for females. This difference in

visual acuity prognosis between sexes cannot be explained by a different distribution of cases with retinopathy as this is the same for both males and females.

The elevation of blood pressure has been correlated by some authors with the deterioration of visual acuity in diabetes. Division of the present group on the basis of blood pressure indicated that in those patients in whom the systolic blood pressure exceeded the norm by more than 10 per cent the visual acuity was definitely worse than those with normal or only slightly (less than 10 per cent) elevated blood pressure.

The deterioration of the visual acuity in the great majority of diabetics was due to retinopathy. Diabetic cataract was found in 4 to 6 per cent and is of secondary importance as regards vision. An earlier study by T. Kornerup (Acta med. Scandinav. 1955, *153:* 81) indicates that lens opacities of all types and severity were found in 14.5 per cent of diabetics. Of those more than fifteen years of age, 3 per cent could not be permitted to drive automobiles because of cataract.

Comment: Considerable emphasis has been placed upon the increasing incidence of retinopathy in diabetics. Ophthalmologists usually see a distorted group of retinopathies, namely those that impair vision. The true visual prognosis in diabetes is thus difficult to estimate from clinical experience.

This report of Kornerup on a large series of nonselected cases of diabetes reveals that although almost half of the patients had retinopathy, the mean values for visual acuity do not justify the pessimism of so many clinicians. The frequency distribution curves for these patients are not included in this paper, but only some 3.3 per cent of the patients were blind. These statistics are of evident practical importance to all physicians handling diabetic patients.

BERNARD BECKER

THE ADRENAL CORTEX IN DIABETIC RETINOPATHY: URINARY 17-HYDROXYCORTICOSTEROID EXCRETION STUDIES

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Bull. Johns Hopkins Hosp., 1956, *99:* 16–22

The hypothesis that diabetics without retinopathy possess a zona fasciculata which is less active than that in normal persons, while diabetics with retinopathy possess one that is overactive, has been discussed in previous reports from the Wilmer Ophthalmological Institute. The findings upon which this hypothesis was based were (1) general clinical observations; (2) changes in the status of the retinopathy resulting from a decrease of either hypophyseal or adrenal

function; (3) histopathologic evidence showing a relative adrenal hypertrophy and increased lipid vacuolization of the zona fasciculata found at autopsy in diabetics with Kimmelstiel-Wilson renal involvement, and similar kidney lesions found postmortem in a patient who had received massive doses of cortisone and ACTH for an orbital pseudotumor; and (4) the finding that 40 per cent of diabetics without retinopathy failed to respond by a significant eosinophile drop to an intramuscular dose of 25 mg. of corticotropin, whereas patients with retinopathy responded uniformly to this dose, as did healthy, normal controls. Added support was given to the theory by the experimental production of lesions resembling the Kimmelstiel-Wilson nephropathy in normal and diabetic rabbits by the administration of intramuscular cortisone, in alloxan diabetic animals by ACTH given intramuscularly, and in a dog made diabetic for five years by the administration of anterior pituitary extract. Moreover, the blood levels of 17-hydroxycorticorticosteroids (17-OH-CS) have been reported to be increased in insulin coma.

In 1953, when a more reliable analytic procedure for measuring urinary 17-OH-CS became available, it was decided to test this hypothesis in a more direct manner. Measurements were therefore made of the daily urinary 17-OH-CS excretions, the diurnal variations in the excretion of these steroids, and the recovery of a standard test dose of 17-hydroxycorticosterone (Compound F) in normal patients and in diabetics with and without retinopathy. The data obtained by these studies show that diabetic patients with retinopathy excrete a significantly larger amount of urinary 17-hydroxycorticosteroids in 24 hours than diabetic patients without retinopathy. There is no significant difference between either diabetic group and the normal controls. Similarly, there is no difference in the urinary diurnal 17-OH-CS excretion pattern among the three groups. Finally, the diabetic group as a whole shows a significantly smaller urinary 17-OH-CS excretion after an oral test dose of compound F than do normal controls. These results neither prove nor disprove the validity of the theory that adrenal function is a causal factor in the production of diabetic retinopathy. Further advances in the study of adrenal function must be made before this problem can be solved. Presently, however, the possibility that the microaneurysms of the diabetic retina and the microaneurysms of the diabetic glomerular vessels, which are probably the primary vascular lesions, may be indicative of an abnormality in mucoid metabolism is being investigated.

Comment: For the past 10 years at the Wilmer Ophthalmologic Institute efforts have been directed toward eliciting measurable differences between diabetics with and without retinal lesions. It was the hope of Dr. Friedenwald that such findings might help to elucidate the basic metabolic defect underlying the retinopathy of diabetes. The early findings of such studies led to a workable hypothesis which implicated the adrenal cortex in the pathogenesis of diabetic retinopathy. Although this hypothesis remains unverified, it still provides a convenient and consistent explanation for much of the data available.

The present paper reports significant differences in average daily urinary excretion of 17-hydroxycorticosteroids between the two groups of diabetics. Individual daily excretion patterns revealed large fluctuations from day to day, especially in the retinopathy group.

In these patients hydroxycorticosteroid excretion reached grossly abnormal levels on some days. These findings are consistent with the adrenal hypothesis. However, as pointed out by the authors, the findings do not conclusively prove the causal relationship of adrenal function to the production of this disease process.

The present report does not answer questions as to possible qualitative differences in steroid production in diabetics, especially those with retinopathy. It is hoped that additional studies will approach this problem as well as the possible alterations in the handling, conversions, and detoxifications of steroids in both groups of diabetics.

BERNARD BECKER

FUCHS SYNDROME, BARRÉ-LIÉOU SYNDROME, AND LESIONS OF THE CERVICAL SPINE

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Ann. ocul., 1956, *189:* 380–390

Fuchs' syndrome, which is well known to ophthalmologists, is characterized chiefly by three major symptoms: heterochromia of the iris, precipitates on Descemet's membrane, and cataract. It has seldom been described as a complication of the posterior cervical syndrome of Barré-Liéou, the symptoms of which are attributed by most authors to vasomotor disturbances of the bulbo-protuberantial region resulting from irritation of the vertebral nerves or generally of the sympathetic plexus surrounding the vertebral artery. The bulbo-protuberantial region is vascularized by the vertebral arteries and the arteries of the lateral part of the region aforesaid are more delicate and therefore more sensitive to vasomotor reactions.

The symptoms of the Barré-Liéou syndrome, which concern chiefly the nervous system, the ears, and the eyes, are well known but often pass unrecognized by specialists in the three branches when they are consulted by patients complaining of retrobulbar pain, buzzing in the ears, headache, and vertigo. Headache and vertigo are the principal neurologic symptoms. The headache, which may be continuous or may occur in attacks, is localized above all in the occipital region with radiation towards the nape and the eyes. The attacks of vertigo are usually short, varying in length from a few seconds to a few minutes. As a rule they accompany the headache. Liéou distinguished two forms: (1) a simple feeling of instability and (2) a feeling of genuine vertigo. The results of vestibular tests are generally normal. So far as the ears are concerned, the patient complains of buzzing sounds and sometimes of earache. Ocular symptoms consist of fatigue without any particular signs on objective examination, retrobulbar pain, and sometimes a decrease in pressure in the central retinal artery. Other symptoms of

a secondary character sometimes seen in the Barré-Liéou syndrome are facial pain, vasomotor crises and spasms of the face, neuralgia of the shoulder, and pseudoangina pectoris, pharyngeal disturbances, transient aphonia, and psychic disturbances (anxiety, fatigue, and psychopathy). All of these various symptoms of the Barré-Liéou syndrome can be explained by the action of the lesions of the cervical spine on the sympathetic plexus of the vertebral artery.

The Fuchs syndrome, which the author has been studying for several years, is in his opinion due, not to inflammation, but to vasomotor disturbances the existence of which is substantiated by the discovery of sclerotic lesions of the vessels and stroma of the iris found on microscopic examination in 21 cases. The coexistence of the two syndromes was first described by Paufique and Chavannes in 1946. Streiff, too, reported a case of typical Barré-Liéou syndrome associated with Fuchs' syndrome and lesions of the cervical spine. In his own series of 55 patients with Fuchs' syndrome, some of whom have been followed for more than 10 years, the author has seen 11 who also had a complete or partial Barré-Liéou syndrome. Moreover, 32 of the patients had marked sensitivity of the nervous system (anxiety, phobias, vasomotor disturbances), and this fact tends to support his theory of the pathogenesis of Fuchs' syndrome. The coexistence of Fuchs' syndrome with the posterior cervical syndrome of Barré-Liéou is in general an expression of the lesions of the cervical spine which are found in two-thirds of the cases of Barré-Liéou syndrome and which play an important part in the pure Fuchs syndrome, although they are less well known in connection with it. Radiologic examination of 40 of the author's patients with Fuchs' syndrome revealed that 23 had lesions of the cervical spine resembling those found in the Barré-Liéou syndrome. In general, the first three cervical vertebrae were untouched but lesions of C5 and C6 were common; the cervical column was rigid; and spondylolisthesis, alterations in the intervertebral space, osteophytosis of the last cervical vertebrae, and decalcification were observed. Radiologic examination of 10 of the 11 patients who had both Fuchs' syndrome and Barré-Liéou syndrome showed involvement of the cervical spine in 7.

Fuchs' syndrome rarely appears as a purely ocular syndrome, and the particular state of the nervous system in patients with this condition, coupled with the frequency of the cervical spine lesions, seems to show that these factors play a major part in its development. Just as the Barré-Liéou syndrome involves the three specialties of neurology, otology, and ophthalmology, so Fuchs' syndrome should be considerered a general neuro-ophthalmologic syndrome. It would be well if neurologists, in examining the pupillary reflexes of their patients, would make it a point to look for heterochromia of the iris, since its discovery would suggest Fuchs' syndrome, leading to examination of the cervical spine and so perhaps to early diagnosis of an unsuspected Barré-Liéou syndrome.

Comment: Because of the paucity of information about this syndrome of Barré-Liéou in both the neurologic and ophthalmologic references Dr. John Holt of our radiology department was consulted with regard to the roentgen ray changes which are listed as well as illustrated in the original article. The changes noted were those commonly referred to as cervical spondylosis in the radiologic literature. This usually is accompanied by pain

in the base of the neck, down one or both arms, and with parasthesias in the ulnar distribution. There may also be referred pain to the occiput. The narrowing between C5 and C6 is commonly seen in at least one half the population over 50 years of age. Dr. Henry Miller, in discussing cervical spondylosis (Proc. Roy. Soc. Med. *49*, Nov. 22, 1955) states that the radiologic changes of cervical spondylosis seem to be merely a sign of middle age perhaps somewhat more reliable than the finding of gray hair, and that the large majority of patients with radiologically significant cervical spondylosis are asymptomatic. Therefore one is forced to conclude that the percentage of roentgen ray findings noted in the present paper is no more significant than the ratio in the population at large.

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THERAPEUTICS

PIGMENTARY DEGENERATION OF THE RETINA DUE TO A MEDICAMENT

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Ophthalmologica, 1956, *131:* 296–303

A new drug, N.P. 207, produced by the firm of Sandoz has been found to have a harmful effect on the pigmented epithelium of the retina. This drug, which resembles chlorpromazine (Largactil) in its general composition but differs from it in having a lateral chain containing piperidine, was distributed to various psychiatric hospitals for use in clinical trials. Its therapeutic qualities were praised unanimously by all the psychiatrists who used it. It was better tolerated than Largactil and it did not produce the Parkinsonian disturbances, disturbances of accommodation, and other side-effects that accompany the use of Largactil in psychiatric doses.

Its injurious effect on the retinal pigmented epithelium was discovered by chance in May, 1955, when several patients in the University Psychiatric Hospital of Zurich, who had been undergoing treatment with it for some months, complained of difficulties of adaptation on returning to the house from the garden. One of these patients, who was particularly hemeralopic, was referred to Verrey and proved on examination to have a typical salt-and-pepper appearance of the eye grounds. At first it seemed that the lesions might have antedated the use of the drug and that it had merely accentuated the patient's subjective symptoms. Examination of other hemeralopic patients treated with N.P. 207, however, revealed five additional cases, indicating a cause-and-effect relation between the drug and the pigmentary degeneration in question. The firm of

Sandoz was informed of the facts and immediately passed the information on to all the clinics making use of the drug. Although the lesions varied from place to place, the Zurich findings were confirmed by ophthalmologic examinations made at the other clinics.

The picture portrayed by the statistics now available is probably incomplete, because the condition will doubtless continue to develop for some time. The patients treated with N.P. 207 fall into three groups: (1) those with definite lesions; (2) those in whom injury is slight or merely suspected; and (3) those without injury. Classification of the three groups according to the dosage given shows that (1) 7 patients who received more than 30 gm. (in daily doses of from 800 to 1000 mg. for several days in succession) were definitely affected; (2) among 14 patients who received from 20 to 30 gm., 3 were definitely affected and 5 were suspected of having injuries; and (3) among those who received less than 20 gm., the only one who was definitely affected had had almost 19 gm., while 8 who were in the suspected group had had large daily doses for several consecutive days.

The hemeralopic condition which first attracted attention might have gone unnoticed in many cases without a systematic examination because, under the influence of the drug, the patients lost aggressiveness and were relieved of anxiety, so that it did not occur to them to complain of their symptoms. Adaptation, visual acuity, and the visual field were notably reduced in many cases. The functional disturbances preceded the eye-ground pigmentation. The retinal lesions developed in three stages: (1) watered reflections in certain sectors of the fundus; (2) fine lesions creating a pepper-and-salt appearance, variously distributed over the fundus; and (3) the same lesions now strongly pigmented and appearing as small black spots.

Apart from the diminution of visual function, which gravely handicaps the therapeutic use of N.P. 207, the problems posed by the selective action of this drug on the retinal pigmented epithelium are highly interesting. They recall the problems connected with the analogous use of septoiode, one of the ingredients of which, sodium iodate, also caused retinal lesions. There must be various endogenous or exogenous factors in the patient that favor the appearance of the degeneration, and they should be systematically sought for.

Treatment with N.P. 207 in these patients was immediately discontinued, and they were given vasodilators and vitamin A. Vitamin E might also logically be used, since it prevents the appearance of lesions in the rabbit when given before sodium iodate.

Comment: This important observation by Verrey concerning the pigmentary degeneration of the retina associated with the use of a new drug, N.P. 207 (Sandoz), has been confirmed by others. Goar and Fletcher, at the American Ophthalmological Society, June, 1956, studied 34 cases who were receiving the drug at the Neuro-Psychiatric Division of the Jefferson Davis Hospital. Of these, 9 had severe visual impairment, 5 minor, and 10 mild. The first symptom was blurred vision occurring within two to five weeks after treatment started. At this time, there were no recognizable signs and several cases were diagnosed as hysteria. Then they noted dilatation of arteries and veins, irregular retinal

reflexes and hyperemia of the nerveheads. With the decreased visual acuity, there were significant cuts in the visual fields. At this time, pigmentary changes were noted in the fundus periphery. With cessation of therapy, a number of these individuals showed improvement in visual acuity and visual fields. There seemed to be some correlation with the onset of this complication and the dosage and duration of therapy. Both of these reports point out the great care which must be exercised before releasing any agent for human consumption. Unfortunately, not all toxic effects will be uncovered by animal experiments. Rucker and his group at the Mayo Clinic failed to demonstrate any retinal pathology with large doses of these agents administered to small experimental animals.

The administration of any new agent for evaluation carries with it a great responsibility for the investigator. The rapid pace at which new drugs are being marketed for clinical use makes it necessary that every ophthalmologist be prepared to evaluate the mass of unsubstantiated claims that are often made for new drugs and to weigh critically the published literature on the properties and actions and applications of the new therapeutic agents in comparison with the older, well-established compounds of the same class.

The mechanism by which N.P. 207 produces these retinal changes is not known. It does resemble the action of sodium iodate in some regard. Further studies along this line may be elucidating.

IRVING H. LEOPOLD

THE EFFECT OF ISONIAZID IN EXPERIMENTAL CORNEAL TUBERCULOSIS

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When mice are inoculated intracorneally with *Mycobacterium tuberculosis* there is a latent period of about 10 days before lesions begin to appear. When such mice are treated with isoniazid (0.3 mg. per mouse per day), starting on the day of inoculation, no macroscopic lesions appear during the period of treatment. When the treatment is stopped at the end of 28 days there is again a latent period of some 10 days during which the cornea remains clear; lesions then begin to appear and progress rapidly.

It would thus seem that the treatment keeps the infection in abeyance but does not eradicate it, and that the development of a macroscopic lesion requires a certain latent period which is of the same order whether it occurs from the time of inoculation or from the cessation of isoniazid treatment.

When, however, larger doses of isoniazid are given during the period of treatment (3.0 mg. per mouse per day) withdrawal of the drug is not followed by the development of lesions after a short latent period, and the cornea remains macroscopically clear for a longer time; in some mice lesions then begin to appear

and develop to involve much of the cornea. Hence, the more intensive treatment has produced, in some way, an effect which keeps the infection in abeyance for a longer period.

The changes which occur in the corneas of mice inoculated intracorneally with *M. tuberculosis* and treated orally with isoniazid have been studied by means of the phase contrast microscope. The treatment does not interfere with the initial cellular invasion of the cornea, but organisms do not multiply appreciably within the cells during the period of drug administration. When the dose of isoniazid is 0.3 mg. per mouse per day, cessation of treatment is followed by bacterial multiplication and the appearance of a macroscopic lesion within a period of some 10 days, i.e., the same as the latent period before the appearance of a lesion in the untreated animals. When the dose of isoniazid is 3.0 mg. per day the lesion appears a good deal longer after cessation of treatment.

Possible explanations for this difference have been investigated. It has been shown that: (a) Treatment with the larger dose of isoniazid for 50 days has not affected the virulence of the organisms remaining in the cornea after this time. (b) When the development of a lesion is prevented by the administration of isoniazid (in either dose), inoculation of the second eye leads to the development of a normal lesion. Such a lesion does not develop in the second eye when the first infection remains untreated. Hence the isoniazid-controlled infection of the first eye failed to confer any systemic immunity. (c) When the cornea of a mouse treated with 0.3 mg. isoniazid per day is removed from the animal and put into Kirschner's medium rapid multiplication of the organisms *in situ* can be demonstrated. When a similar experiment is performed with a cornea of an animal treated with the larger dose of isoniazid such rapid multiplication is not observed.

One of the most important problems in the chemotherapeutic treatment of tuberculosis is the frequent failure of drugs to eradicate the organisms from the body. Though such treatment is, as a rule, strikingly successful in the control of signs and symptoms, the disease relapses in many patients at various times after cessation of drug administration. The present experiments help to throw some light on what is happening in such lesions, though they are not concerned with drug resistance, which is an important factor in the control of human disease.

In the first place they show that prolonged treatment with isoniazid, though it checks the multiplication of the bacilli, does not kill all of them. They remain visible in macrophages, mostly as small, thin bacilli, presumably a resting form; and on cessation of treatment they can start multiplying again, as is demonstrated by growth in Kirschner's medium and also by the subsequent development of typical lesions in the cornea. Another point of interest is that, as the duration of isoniazid therapy increases, the extent of the microscopic corneal lesion gradually decreases; this involves not only a decrease in the diameter and thickness of the aggregate of cells which make up the lesion but also a decrease in the density of the cell population, so that as time elapses cells become individually visible, whereas at the beginning of treatment the dense packing of the cells

within the lesion made it possible to see any detail under the phase contrast microscope. What happens to the cells which disappear from the lesion and, more important, to the bacilli which they presumably contain? The duration of life of such cells is in all probability quite limited and thus they must break down, liberating the bacilli which they contain. Such bacilli may then (1) die and disintegrate and this may of course also happen while the bacilli are still within cells; (2) be carried away to other parts of the body where they may be dealt with; or (3) be taken up by macrophages within the lesion, thus increasing the population of bacilli per cell. This third possibility is not supported by what we have seen by the examination of lesions under the phase contrast microscope, for there was no suggestion of any increase in the number of bacilli per cell.

Comment: This study demonstrates very clearly the difficulties encountered in the chemotherapy of tuberculosis. One of the primary difficulties is the rather frequent failure of drugs such as isoniazid to eradicate the organisms from the body. The study indicates that, with the cessation of therapy, experimentally induced lesions will flare at varying periods of time depending on the dose of isoniazid which had been employed to suppress the development of the lesion. The virulence of the organisms does not seem to be affected by the medication. The immunity of the animal, however, is altered by the administration of isoniazid. It appears that the administration of isoniazid interferes with the naturally developing immunity against initial infection with tuberculosis induced in the cornea. The study stresses the possibility of relapse occurring in human tuberculosis after cessation of treatment with drugs such as isoniazid. Therapy continued for as long as 50 days did not prevent the subsequent development of lesions after the cessation of therapy. This phenomenon has been encountered in human tuberculosis and reported previously in experimental lesions with ocular tuberculosis. It stresses the importance of very prolonged therapy with antituberculous drugs when one suspects a tuberculous etiology in ocular inflammations.

IRVING H. LEOPOLD

HEREDITARY DISEASE

GENETIC PROGNOSTICATION AND COUNSELING IN OPHTHALMOLOGY

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Tr. Am. Acad. Ophth., 1956, *60:* 576–586

The number of requests being received by physicians for genetic prognoses in specific types of ophthalmic disease is rapidly increasing. Heredity clinics or counseling centers have been established in more than a dozen leading medical universities and institutions and are now able to offer the public professional advice based on a sound foundation of active research, experience, and teaching.

A physician who is to provide sound advice in problems involving hereditary ocular disease must meet certain requirements.

(1) He must possess a thorough and workable knowledge of the principles of general genetics, based not only on careful study and assimilation of these principles as applied to laboratory material, but also on actual experience in applying them to human data.

(2) He must be a well-trained and experienced diagnostician capable of making an accurate diagnosis of ocular conditions.

(3) He must have a familiarity with the literature relating to specific ocular traits that will enable him to interpret the interfamilial and intrafamilial variations of human genetic traits, as well as their usual modes of transmission.

(4) He must be able to draw up a careful and accurate pedigree of the family in which a given trait is being studied, basing it on examination of all the available members of the family and avoiding the error of relying on hearsay evidence. In this connection, it should be remembered that the same clinical trait may be transmitted by different hereditary patterns of transmission in different families. All the following modes of inheritance, for instance, have been reported for retinitis pigmentosa—without other systemic association: (a) simple autosomal recessive, (b) simple autosomal dominant, (c) sex-linked recessive, (d) partial sex-linked recessive, (e) partial sex-linked dominant, and (f) intermediate sex-linked.

(5) He must be careful to obtain a detailed history of the pregnancy from the patient's mother whenever possible, because noxious agents, acting during intrauterine development, may lead to ocular pathologic changes indistinguishable from those of genetic origin. Clinically the result is a confounding of genetic disease with a similar but environmentally induced disease (the so-called phenocopy).

(6) He must also have a feeling for the sensitivities, attitudes, and environment of the client, and be able to evaluate the relative importance of the trait

being studied, in the light of its economic, sociologic, psychologic, and cosmetic significance.

Ocular genetic counsel becomes extremely difficult when one is confronted with a sporadic case of congenital or developmental disease (i.e., one in which the patient's parents and siblings are normal for the specific trait or disease being studied). In such cases four possibilities must always be kept in mind:

(1) The specific anomaly may have been the result of a mutation in the germ-plasm of one of the two parents. Contrary to most medical opinion, mutation is a very common source of ocular pathologic change.

(2) The sporadic disease may have been produced by the action of a noxious intrauterine agent.

(3) The anomalous trait may have been the result of the homozygous state of a recessive gene. In such case it would have been necessary for each parent to have contributed a similar abnormal gene, thus giving the affected child a double dose (or, as it is said, the child is homozygous for the specific gene). Since closely related mates are most likely to possess like rare recessive (hidden) genes, the question of consanguinity is of the utmost importance in the diagnosis of such recessive disease states.

(4) Failure of penetrance of the gene is a vagary of human inheritance patterns that should always be kept in mind and explained to the client. Certain simple autosomal dominant genes (e.g., those determining ectopia lentis) may fail to exhibit phenotypically their presence in the germ-plasm of the individual, and so far as can be clinically determined, they then appear to have skipped a generation.

Information concerning genetic risk figures for most of the common and rare ocular hereditary entities is not yet available. The theoretic evaluation of genetic risk rates for ocular traits implies merely the application of Mendelian principles in an attempt to estimate the probability that an individual will inherit or transmit a specific altered gene.

As a guide to further study, the author presents a list of ocular disorders, both commonplace and rare, classified according to their mode of inheritance as dominant, recessive, sex-linked recessive, and intermediate sex-linked.

In the dominant ocular diseases and defects, the genetic risk factor for children of an affected parent is theoretically one chance in two, or 50 per cent. This will be reduced, of course, if the gene is not fully penetrant. In the case of recessive traits, the affected individual is presumed to be homozygous for the gene (double dose). The genetic risk that subsequent siblings of the affected person will be similarly affected is one in four, or 25 per cent. In the case of sex-linked recessive traits, all the daughters of an affected male may be assumed to be carriers for the trait and thus capable of transmitting the gene to 50 per cent of their male offspring, who will be affected. The daughters of carrier females have a 50 per cent risk of being carriers in their turn. Intermediate sex-linked inheritance results in all the daughters of an affected male's becoming carriers of the trait; in addition, they show a detectable clinical change. Male offspring of carrier females have a one-in-two chance of being affected and their daughters, a one-in-two chance of being carriers (50 per cent risk).

Basic Sciences

ANATOMY

THE RELATIONSHIP BETWEEN NEUROHISTOLOGY AND CORNEAL SENSIBILITY

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Brain, 1956, *79:* 119–159

Between 1894 and 1896 Von Frey brought forward evidence in favor of the view that it was both possible and desirable to apply Muller's laws of "specific nervous energies" to each of the four "primary modalities" of common sensibility—touch, warmth, cold, and pain. The theory was attractive, for clinicians had long maintained that under pathologic conditions any one of the primary modalities might be lost while the remainder were apparently unaffected. The most compelling arguments in favor of the specificity of sensory nerve fibers and endings arose from observations on corneal sensibility. Pain was the only sensation which could be evoked from the cornea, and free nerve endings only were found in this situation. By contrast, cold as well as pain could be evoked readily from the conjunctiva, particularly at the limbus. In this situation Von Frey and his colleagues accepted and later apparently confirmed that there were numerous Krause end bulbs.

However, Weddell and his colleagues have recently drawn attention to the impossibility of equating the four commonly recognized modalities of cutaneous sensibility, touch, warmth, cold and pain, with four morphologically distinct kinds of nerve termination *in the skin*. For this reason it was considered desirable to reexamine the evidence relating to corneal sensibility.

The innervation of the human cornea, it now seems reasonably certain, takes the following form. Bundles of nerve fibers approach it in a radial manner from the limbus. There are about 1,200 nerve fibers, but whether this number represents the number of trigeminal nerve sensory ganglion cells involved is uncertain, although little collateralization takes place among axons in the region of the limbus.

The majority of nerves, all of which are unmyelinated but surrounded by Schwann elements, after dividing the subdividing repeatedly, pierce Bowman's membrane, giving rise to a wisespread arborization of naked axoplasmic filaments which at first lie between the membrane and the basal layer of epithelial cells but eventually send branches which pass up into the epithelium and apparently terminate freely between the cells in all layers, including those close to the corneal surface. A few nerve fibers surrounded by Schwann elements leave the

bundles lying within the cornea at intervals and give rise to endings in the substantia propria.

The statement that pain is the only sensation that can be evoked from the cornea can be found in current physiologic and clinical textbooks. Despite evidence to the contrary, this authoritative enunciation of Von Frey and apparent confirmation of an appealing theory were so compelling that his views were easily and readily accepted.

The following stimulus objects were selected:

(1) Nylon sutures of three different thicknesses.

(2) A solid copper cylinder maintained at predetermined temperatures, the end of the cylinder being shaped so as to make a complete and even contact with the central part of the cornea.

(3) An apparatus selected to deliver jets of air at selected temperatures onto the surface of the cornea.

(4) Infrared radiation of between 1 and 3 μ wave length through an appropriate filter.

Observations were made to 10 subjects. Reports relating to touch were evoked by the finest nylon suture brought into brief contact with the surface of the cornea. No reports of pain could be elicited with this stimulus object. Reports re ated to warmth were consistently evoked by a brief contact with the copper cylinder at a temperature of 1.5°C. higher than the cornea, by jets of warmed air, and by infrared irradiation. Reports of cold were elicited by the copper cylinder and cabled jets of air.

Reports of pain were consistently evoked when a heavier nylon suture than that eliciting touch was brought into contact with the cornea. Such stimuli caused no detectable damage. All of the stimulus objects referred to, when used under similar conditions, evoked reports related to similar sensory modalities when used to stimulate the skin or exposed mucous membrane of the lip.

Comment: This is a most interesting article and one that should promote further investigation into the problems of corneal sensitivity. This reviewer has considered pain to be the only sensation mediated by the corneal nerves because the standard reference works state this most dogmatically. Yet from the clinical viewpoint it is interesting that, following the instillation of a local anesthetic for the removal of a corneal foreign body, many patients will state that they experience the sensation of cold or warmth when the cornea is touched. This has usually been considered an alteration of the corneal sensibility as a result of the instillation of an anesthetic, but this monograph makes this explanation seem very unlikely.

ALBERT N. LEMOINE, JR.

OPTICS

STEREOSCOPIC ACUITY AND THE ROLE OF CONVERGENCE

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J. Optic. Soc. America, 1956, *46:* 269–273

The extent to which proprioceptive reflexes or a kinesthetic sensation of changes in muscle tension from the extraocular muscles of the two eyes aids in binocular space localization—and more particularly in stereoscopic vision—is apparently a problem not yet settled to everyone's satisfaction. Although the carefully planned experiments of Hillebrand and of Bappert seemed to afford striking evidence that accommodation and convergence played little or no part in spatial localization, the more recent discovery of muscle spindles, those end organs found in muscles having a proprioceptive function, in the extraocular muscles of man and certain animals has again raised the possibility of a proprioceptive sense from those muscles. Certainly many physiologists and ophthalmologists hold to the opinion that such a myosensory influence must exist. Chevasse is said to have believed strongly in the existence of a "tension sense," which he thought might be inhibited unless reinforced by the presence of other clues or stimuli to spatial localization. Inhibition of this kind, if it exists, would account for the negative results of such experiments as those of Hillebrand. The present status of the problem was summarized by Irvine in the statement that "the proprioceptive sense of the eye muscles must be relegated to a vague orienting the position of the eyes to the position of the head, with an increasingly greater effect as it is reinforced by other reflexes." Furthermore, it is quite possible that this sense of eye movement may not even reach consciousness in a measurable form.

Much of the marked improvement of stereoscopic depth acuity obtained when eye movements are permitted, as compared to that obtained with a constant fixation, has been regarded by Wright and by Rady and Ishak as evidence that the change in convergence of the eyes plays a part, if not an important one, in binocular depth perception. This supposition, however, has been challenged on the ground that the results on which it is based can be interpreted in terms of visual acuity, or, equally valid, stereoscopic acuity in the peripheral fields. The purpose of this paper is to amplify this interpretation with the presentation of new data.

The apparatus used permits a test object to be varied in different stereoscopic depths, that is, with different disparities between its images in the two eyes and those of a reference object, but without introducing a change in its brightness,

color, or size, or having it go out of focus. Thus empirical clues to the spatial depth are essentially eliminated.

With this apparatus the subject sees a vertical illuminated reference needle, A, and a test needle, B, by reflection from 50/50 movable transmission-reflection mirrors. A rotation of the mirrors introduces a transverse disparity between the images of the test needle relative to the images of the reference needle. The disparity corresponding to the change in rotation of the mirrors can be read directly from a dial indicator on the apparatus. The angular separation of the two needles can easily be changed by adjusting the position of the arms on which the needles are mounted. The reference needle was 50 cm. from the eyes. The subject, with head held in a headrest and a wax bite (or chin cup), observed the needles through appropriate rectangular apertures against a uniform black background which restricted the binocular field of view to these needles. The tests were conducted in an otherwise dimly lighted room.

Although it would have been desirable to present the test sitmuli for only a brief period and to have used a psychometric constant-stimulus procedure, this cannot be done when the subject looks alternately from reference needle A to test needle B. Consequently, both reference and test needles kept continuously visible and a method of adjustment was used in which the subject himself turns the knob that controls the disparity between the images in the two eyes, adjusting it so that the test needle seemed to be as far away from him as the reference needle. Twenty settings were made (1) with constant fixation, and (2) with the subject looking alternately from A to B. Experience showed that changing fixation from A to B in one glancing movement was most frustrating, because the final adjustment was almost like a "constant fixation" on needle B. Hence in the experiments continuous alternating fixations were requested of the subject.

The mean and standard deviations were determined for each group of adjustments, for a series of different separations of the needles. The standard deviation of the settings was taken as a measure of, and as proportional to, the stereoscopic threshold. It is primarily this quantity that is to be compared in the methods of constant and of alternating fixation. When the results of the experiments, repeated several times on different days, were averaged, it was found that adjustments were almost impossible for constant fixation when the angular separation of A and B exceeded 15 arc degrees, apart from the influence of the blind spot. It was not clear to the present subjects how the subjects of the earlier investigators were able to obtain reliable data with angular separations up to 50 arc degrees, which were what they used.

Graphic representation of the results obtained by the three subjects participating in this study shows clearly that the stereoscopic precision is much better for the same separation of objects with alternating fixation eye movements than with constant fixation. Now if one wishes to state how much better stereoscopic acuity is with alternating fixation than with constant fixation for a given separation of the test objects, the ratio of the standard deviations, or the difference, can be calculated. This ratio, or difference, has a practical value, since it states an important fact quantitatively. However, if one wishes to under-

stand the underlying physiologic bases accounting for the results, the ratios of the acuities or even their differences are of little value, especially in trying to resolve the relative role played by disparity between the images in the two eyes, and the role of changes in convergence.

The stereoscopic thresholds of depth perception rests in the final analysis on the peripheral visual acuity of the two eyes. If a subject fixates one of a pair of test objects, the images of the other object will fall peripherally on the retinas of the two eyes. The ability to discriminate differences in disparities will depend on the resolving power of the percipient elements in those regions of the retinas. In fact, one can say that the stereoscopic acuity can be no better than the poorer resolving power of either eye.

When the eyes are permitted to look from a point A to a point B, both eyes will be continuously under the stimuli of both points during the eye movements. Thus the images of both A and B will fall on various parts of the retinas during the movements, but will involve at all times, except for fixations on either A or B, visual acuities (stereoscopic acuities) lower than those at the foveas but higher than those corresponding to the angular separation of A and B with constant fixation at A. Thus, at some intermediate position of convergence between A and B during the movements, the images of both A and B in the two eyes will fall on portions of the retinas where the stereoscopic acuity (visual acuity) will be maximal. For a convergence on either side of this intermediate convergence the stereoscopic acuity for one object will be lower than that for the other.

If the decrease in stereoscopic acuity were the same on both sides of the visual field, one would expect the stereoscopic acuity measured with alternating fixation to correspond to the stereoscopic acuity obtained with constant fixation at one-half the visual angle subtended by A and B. This would represent the maximal stereoscopic acuity possible as a result of the stimulus of retinal disparity alone. Now, if convergence movements, that is, a proprioceptive or a similar sense from the extrensic muscles, contributed quantitatively to stereoscopic acuity, one might expect the stereoscopic thresholds measured to be lower than those predicted from the maximal stereoscopic acuity at one-half the separation of the test objects. In general, however, the actual data, the stereoscopic thresholds, obtained in these studies with alternating fixation are greater than those predicted. Thus the stereoscopic acuity in terms of retinal response in actually less with alternating fixation than with constant fixation.

The conclusions drawn from this study do not preclude a possible distance localization for larger differences in distance by a proprioceptive sense, nor do they preclude the possible existence of proprioceptive reflex and "feed-back" innervations useful in executing accurate fixation eye movements; the essential point here is that this proprioceptive sense dcs not seem to be a factor in stereoscopic depth acuity, where the thresholds of disparity and therefore convergence differences are found to be so small.

Comment: What role kinesthetic sensations, especially convergence and accommodation, play in spatial localization is one of the great problems of visual physiology. Many are

the experiments which make this role rather doubtful. On the other hand, many still hold to the opinion that this part is not negligible. Ogle refers in this paper to one special facet of the problem only, that of the influence of convergence (notably of its changes) on stereoscopic depth discrimination.

Stereoscopic depth acuity is markedly improved when eye movements are permitted during the experiments. This has lately been confirmed by experiments of Wright (Proc. Phys. Soc., London, 1951, *64:* 289) and of Rady and Ishak (J. Optic Soc. America, 1955, *45:* 530), and is once more shown to be the case by the experiments described in this paper. The experimental set-up is remarkably simple and capable of offering accurate data without interference by those extrinsic "experiential" factors which so often mar the results of experiments in space perception. Even more remarkable is the mode in which the experimental findings are evaluated. Ogle uses the mean standard deviations of the adjustments of a linear test target as a measure of stereoscopic acuity under the certainly justified assumption that the size of this is the best measure of the relative accuracy of these adjustments. It turns out that the standard deviations (1) increase in some fairly linear fashion with the increase of angular separation between reference line and test line; and (2) are consistently smaller when eye movements are permitted rather than the reference line bifixated. (By the way, all three observers of this series found adjustments impossible if the separation between the two lines approached 15 degrees, whereas the abovementioned observers obtained what to them appeared to be reliable data up to separations of 50 degrees.) Ogle does not believe, however, that these results—the better acuity of stereopsis for any given separation of targets achieved with moving eyes—is in any way a proof of the influence of convergence and its variations upon depth discrimination. His argumentation is certainly convincing; and one will readily accept the view that the better exploitation of local visual acuities rather than the proprioception of changes of convergences is responsible for the improvement.

These results, of course, do not exclude the possibility that in some other fields of spatial localization, especially in the discrimination of the so-called absolute distance of sensed objects, convergence does play a role. In other words, the angle of convergence (to use Luneburg's nomenclature) might still be a significant parameter of visual localization even if Ogle's discussion has made it highly probable that $d\gamma$ (the change of this angle) might have only negligible effect upon stereoscopic depth discrimination, or, in any event, a lesser effect than Luneburg had assumed.

Indeed, it is this reviewer's firm belief that stereopsis, so-called relative depth discrimination, Panum's areas, physiologic diplopsis are all to be explained on the basis of the peculiar neuroanatomy of the visual cortex and have to do with the momentary position of the eyes. Ogle's discussion only confirms this view.

ARTHUR LINKSZ

Reports from Abroad

SPAIN

TRENDS IN OPHTHALMIC SURGERY

ANESTHESIA

Good anesthesia is essential to the sucess of ophthalmic surgery. It is important to eliminate not only pain, but also preoperative and postoperative anxiety, and the troublesome reflexes of the neurovegetative system. We use the "pharmacodynamic potentialization," a combination of drugs which produces marked "organic quietness." This combined anesthesia (Bellergal, Fenergan, Demerol, Diparrcol, Largactyl, and curare) acts upon all levels of the nervous system and inhibits its impulses.

It is fundamental to eliminate active as well as passive congestion of the choroidal and orbital vascular areas which causes sudden increase of the intraocular pressure with the production of complications such as iris prolapse, loss of vitreous, and expulsive hemmorhage. With the above medication, the patient is sedated enough so that the instillation of a solution of 10 per cent cocaine is adequate for anesthesia and infiltration is completely unnecessary.

KERATOPLASTY

It is of the utmost importance to obtain perfect coaptation between the graft and the receptor. For this the following measures are indispensable: The borders must have regular edges. Direct multiple sutures must be very well placed. Technically, it is necessary to have complete "organic quietness" (potentialization), excellent instruments (minimal operative trauma), and special material for the sutures.

Since 1951, we have been using extremely fine virgin silk which permits multiple sutures (12 to 16 sutures), so as to cause no serious operative trauma. Special fine, sharp needles, 4 mm. long (Grieshaber model 83) are used. A special needle holder has been adapted to the delicacy of these needles (J. I. Barraquer-Moner: Grieshaber).

Microscopic control by the use of a slit-lamp allows perfect dissection in lamellar keratoplasties, and the correct placement of sutures. The width, intracorneal tracks, and tension of the sutures can be controlled precisely. The section is more nearly complete and best performed with the trephine because the depth of the anterior chamber is better appreciated. Maximal miosis permits better centering of the trephine, and anterior synechias are more easily prevented. This also minimizes the likelihood of damage to the lens.

A thorough examination of the general health of the patient is important. Focal infection plays a fundamental role and must be eliminated completely.

In the postoperative period, neovascularization is to be prevented. Beta ray therapy, cortisone, hydrocortisone, and antihistaminics, which prevent

inflammatory reaction and incompatibilities between graft and receptor, are used. Postoperative manipulations are carried out in the operating room, under the microscope with the patient under potentialization. The sutures are taken out at repeated steps, from the fifteen postoperative day to the twenty-fifth to thirtieth post-operative day. Antibiotics are administered prophylactically together with Diamox to produce a postoperative hypotony which makes coaptation easier.

CATARACT

Prophylaxis of complications by the use of antibiotics, anti-inflammatory drugs, and potentialization permits us to perform bilateral cataract operations at the same operative time, one eye immediately after the other. Thus, without an increased risk of complications, both transparent lenses in myopias of over 18 diopters may be removed to correct the error of refraction and to improve vision.

The procedure indicated in patients over 21 to 30 years of age is phakoeresis extraction with a large semispherical cup with a variable vacuum combined with tumbling. For this operation, the following steps are fundamental:

(1) Muscular, psychic, and neurovegetative relaxation (potentialization).

(2) Ample corneosclero-conjunctival incision (half a cornea).

(3) Peripheral iridectomy (not iridotomy).

(4) Previous suture with virgin silk, corneoscleral, subconjunctival.

(5) Vacuum regulated between 40–50 mm. Hg according to the age of patient and type of cataract. (Young patients with a stronger zonule require a greater vacuum than older patients.)

(6) Application of the cup on the lens capsule, without exerting pressure on the lens.

(7) When a vacuum is produced, the operator lifts the cup and with this, the lens. At the same time, a contrapressure is exerted with a forceps at the limbus (at 6 o'clock). Extraction then goes on with tumbling, while a gentle pressure with the forceps accompanies the maneuver.

(8) Complementary sutures and irrigation of anterior chamber with acetyl choline solution, 1:10,000 to produce maximal miosis. A solution of plasma and thrombin is then applied to fix the conjunctival flap. The advantages of this technique are complete lens extraction in 90 to 95 per cent of the cases, and loss of vitreous in less than 1 per cent of the cases.

In patients less than 25 years of age, as the zonule is very strong, extracapsular extraction is carried out in three stages: (1) wide discision of the anterior capsule; (2) extraction of intumescent masses; and (3) capsulotomy after six or eight months (posterior capsule opacities in most cases.)

We have not observed any increase in retinal detachment in myopes, when an *extraction without complications* has been performed.

INTRAOCULAR ACRYLIC

Alloplastic cornea. This is indicated after the repeated failure of keratoplasties. The "shirt-button" model (Figure 1) is the one of election. In one case, following

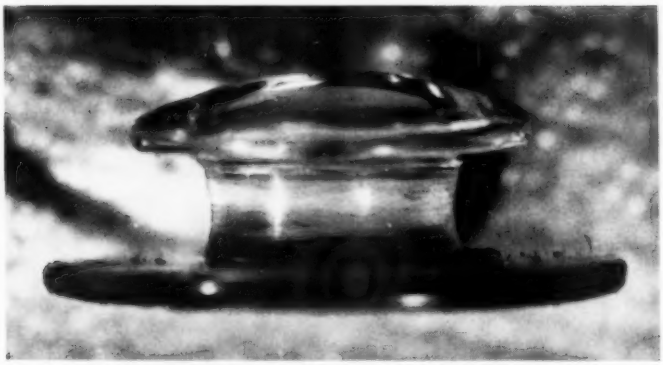

FIGURE 1. The alloplastic cornea of "shirt-button" shape

surgery and after nine months' observation, there was good tolerance and vision. In another case following surgery and after three months' observation there was good tolerance with poor vision due to an old chorioretinal lesion.

Lenses in anterior chamber. The indications include:

(1) Correction of anisometropias for (a) optical correction in monocular aphakia (convex lens); (b) optical correction in high monocular myopia (concave lens).

(2) Correction of binocular ametropia.

Strampelli's lenses are used. They are specially made to fit the refraction error of the patient and the diameter of the anterior chamber of each eye. With maximal miosis, a corneal incision is made in the superior temporal quadrant. The lens is introduced in the horizontal position and the wound closed with two or three sutures. A peripheral iridectomy must be made to insure communication between posterior and anterior chamber. It is to be placed far away from the tip of the lens to prevent blockade by the lens.

The advantages of this technique are perfect tolerance and close correction of the ametropia. There is no postoperative inflammation, as the technique is simple. There is no hypertension as the lens rests only in the angle on three points. This prevents luxation of the lens. If the posterior capsule is opaque, discision can be easily performed. The lens can be inserted in eyes with the normal lens in position. Seventy cases have been operated from June, 1954, to August, 1956; there has been perfect tolerance in all and very good vision.

We have placed Ridley's lens in the retroiridal space in more than 20 cases. The inflammatory reaction, pigmentary deposits, and opacification of the capsule led us to abandon this technique in 1954. At present, we have removed the lens in several of our cases, substituting the Strampelli lens after three months with good function result.

SCLERAL SHORTENING

Lamellar scleral resection is the technique of choice. In retinal detachment resection is combined with diathermy preferably; and diathermy only is reserved

for good cases only. Without selecting the cases, we have obtained 82 per cent cures. Actually, we are practicing the inclusion of a polyethylene tube in cases of very bad prognosis, with encouraging results (Schepens).

When retinal detachment is not present, the operation may be indicated when there is: (1) progressive reduction of the visual field; (2) increase in the size of the blind spot; (3) diminution of visual acuity; (4) increase in the number of vitreous floaters; and (5) retinal hemorrhages. These disturbances are related to a diseased condition of the choroid and retina (distension and deficient irrigation of blood, etc.). After the scleral resection these disturbances tend to disappear and visual fields and acuity improve.

This operation is particularly indicated to create an artificial "ora serrata," after the extraction of the transparent lens, if the periphery retina is altered or there are posterior lesions in evolution. Furthermore, though the effect of the resection on the dioptric power is small, we obtain with it an improvement of the ametropia and residual astigmatism.

The technique is easy and without danger. The resection is to be practiced as close to the equator as possible, taking care not to injure the vortex veins, and disinserting only one muscle. If necessary, we perform a complete annular resection in two stages, with an interval of three months between procedures.

The operation is completely innocuous for the myopic globe, and we have never had accidents. As of July 1955 our experience includes more than 350 cases, with real improvement in 73 per cent of these cases.

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Book Reviews

Endogenous Uveitis, by Alan C. Woods, M.D. (*The Williams & Wilkins Company, Baltimore. 303 pp. $12.50*), *is a monumental review concerning a subject about which the author has contributed for many years. Here it is reviewed by Henry F. Allen, contributing editor of the Survey of Ophthalmology.*

By Henry F. Allen

This monograph is the outgrowth of a manual originally used by the author as an outline in presenting the subject of endogenous uveitis for the Home Study Course of the American Academy of Ophthalmology and Otolaryngology. An unusual feature of the organization of the subject matter, resulting from its origin as a manual, is its presentation under the headings of the different phases of the uveitis problem—classification, pathogenesis, pathology, diagnosis, and treatment. The volume is replete with references to the current literature, including the author's own contributions to current knowledge of this subject.

In the first few pages the division of all uveitis into the granulomatous and nongranulomatous forms, originally propounded by Woods in 1947, is set forth, which premise, familiar to readers of his papers over the last 10 years, may be summarized as follows: Granulomatous uveitis is believed to be the result of direct infection of the eye by specific causative agents, whereas nongranulomatous uveitis is believed to be the result of a sterile insult—physical, toxic, or allergic. While recognizing that these entities are not always clear-cut and separable on clinical grounds alone, the author defends the use of this broad classification on the basis of its established usage in the literature and of the clinical connotations which the subdivisions have acquired over the years.

The basic and specific symptomatology and pathology of both types is brought out with emphasis upon the role of the large mononuclear phagocytes and epithelial cells in the granulomatous form. The theory of the relation between allergy and immunity in experimental ocular tuberculosis, as developed in the author's long series of papers on this subject, is summarized. A correlation between allergy, immunity, and four clinical types of ocular tuberculosis is then attempted. Syphilis, brucellosis, leptospirosis and leprosy constitute the remaining forms of nonpyogenic bacterial uveitis.

After description of other etiologic types, the pathogenesis of the infectious (granulomatous) and allergic (nongranulomatous) forms of uveitis occupies the remainder of the first chapter.

Symptomatology, clinical signs, and pathology of the various forms are the subject of the second chapter. The scarcity of pathologic material from cases of nongranulomatous uveitis is emphasized.

Etiologic diagnosis, based on a careful history, detailed ophthalmologic examination, complete medical survey, and various laboratory tests, is described in

detail. Positive and presumptive criteria for diagnosis of the various types of uveitis are presented. An elaborate nine-day routine for office management of the etiologic study concludes the third chapter.

Treatment is divided into specific and nonspecific measures and both types are fully discussed in the fourth and final chapter. Dosage regimes for the corticosteroids and other agents are established, and the technique of desensitization by autogenous streptococcal vaccines is described.

A book which represents the lifetime experience of a careful and conscientious observer of clinical and experimental disease in a major field deserves the attention of all ophthalmologists. Whether or not one accepts the author's theories of classification, pathogenesis, and etiology, it must be admitted that they have had a provocative and stimulating effect. Certainly a theory, even if it cannot be proved in minutest detail, is better than no theory at all.

This book will provoke controversy in at least three fields. Virologists will demand confirmation and more concrete proof of the presumed viral etiology of Harada's and Behcet's diseases. Allergists will require specific demonstration of the antigens and antibodies directly involved in the production of alleged hypersensitivity reactions in the eye. The importance of bacterial allergy in uveitis has been questioned by Ashton (Acta Conc. Ophth., 1954, *17:* 1214), whose critique of Woods's theories should be read by all serious students of this subject. Ophthalmologists will recoil from the exhaustive nature and the expense of the proposed etiologic survey in the face of a limited prospect of making a positive, specific, etiologic diagnosis, in any event.

Nevertheless, *Endogenous Uveitis* is an important book. It presents in reasonable form the theories of one major school of thought on this subject. It is a useful reference manual to the current literature and for the interpretation of many laboratory tests unfamiliar to ophthalmologists. Finally, in a field where speculation has been heaped upon surmise, it attempts to create an orderly framework on the basis of a limited body of factual data. The task of expanding that body remains for present and future generations of clinicians and basic scientists.

A lucid style, an attractive format, and a fine series of illustrations enhance the value of this volume. A small number of typographical errors and incorrect Latin endings should be corrected in subsequent editions.

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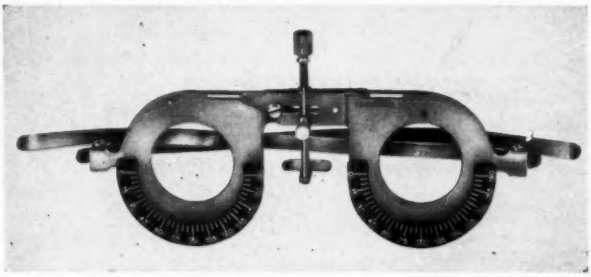

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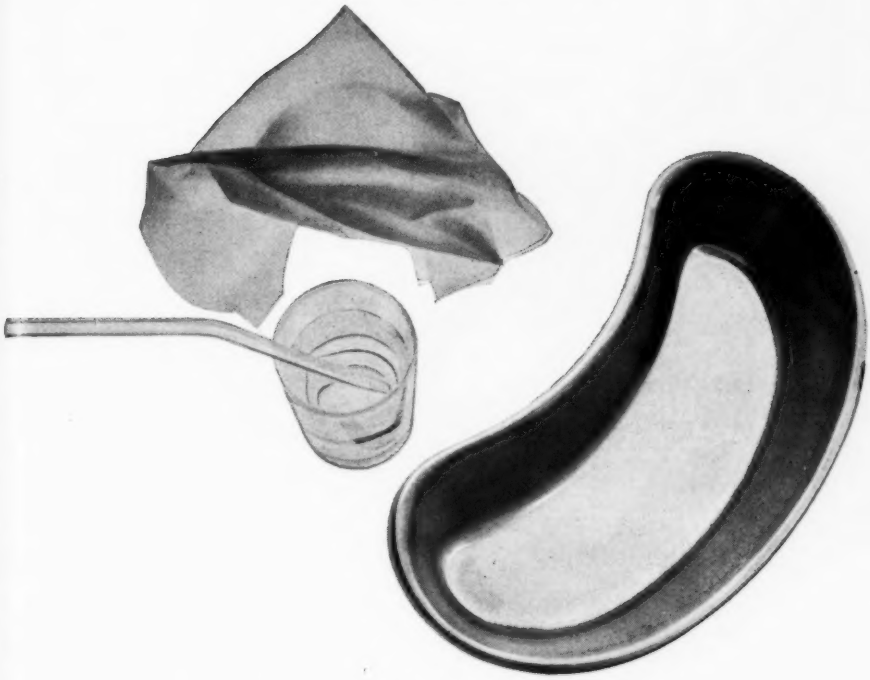

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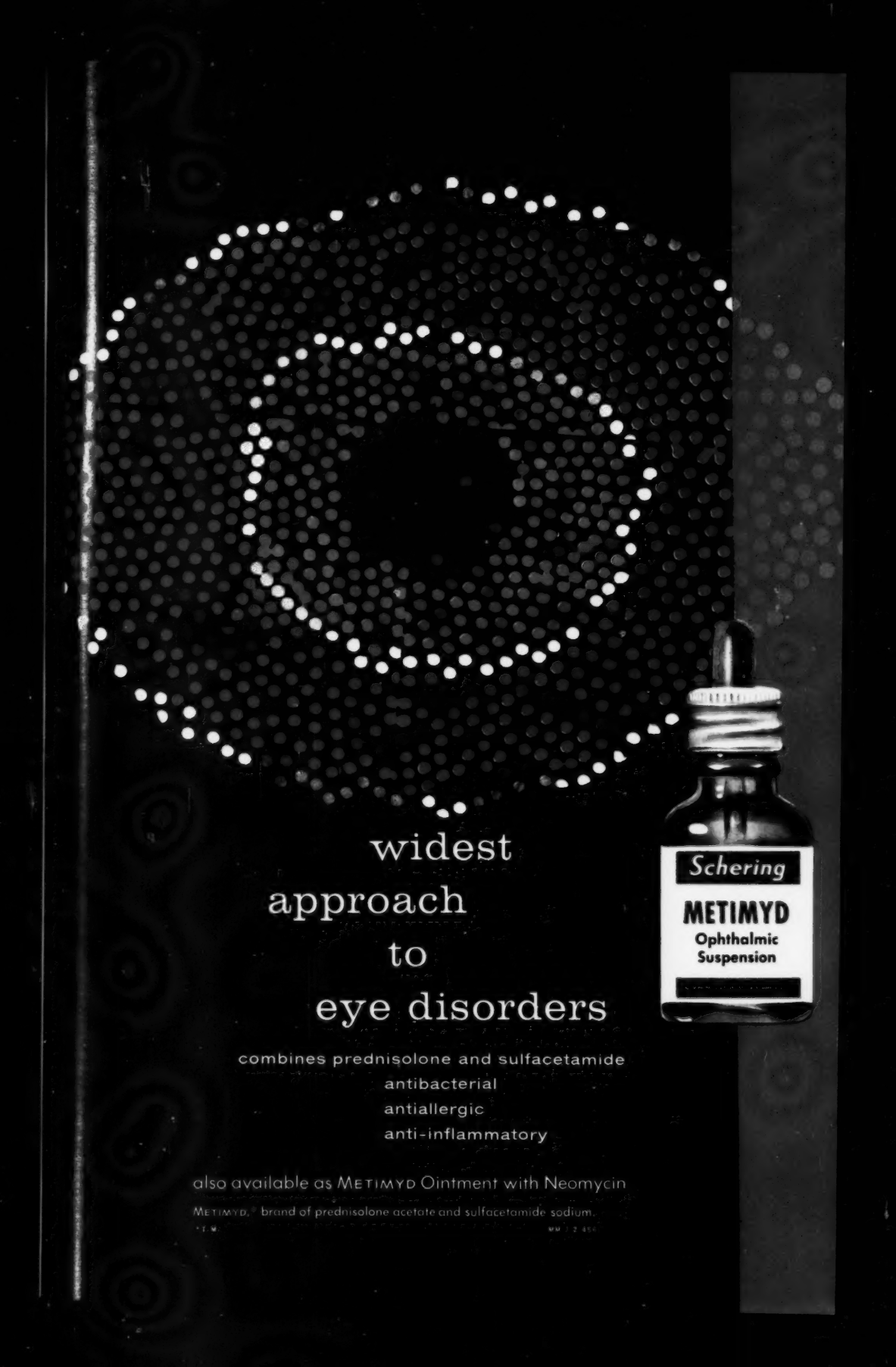
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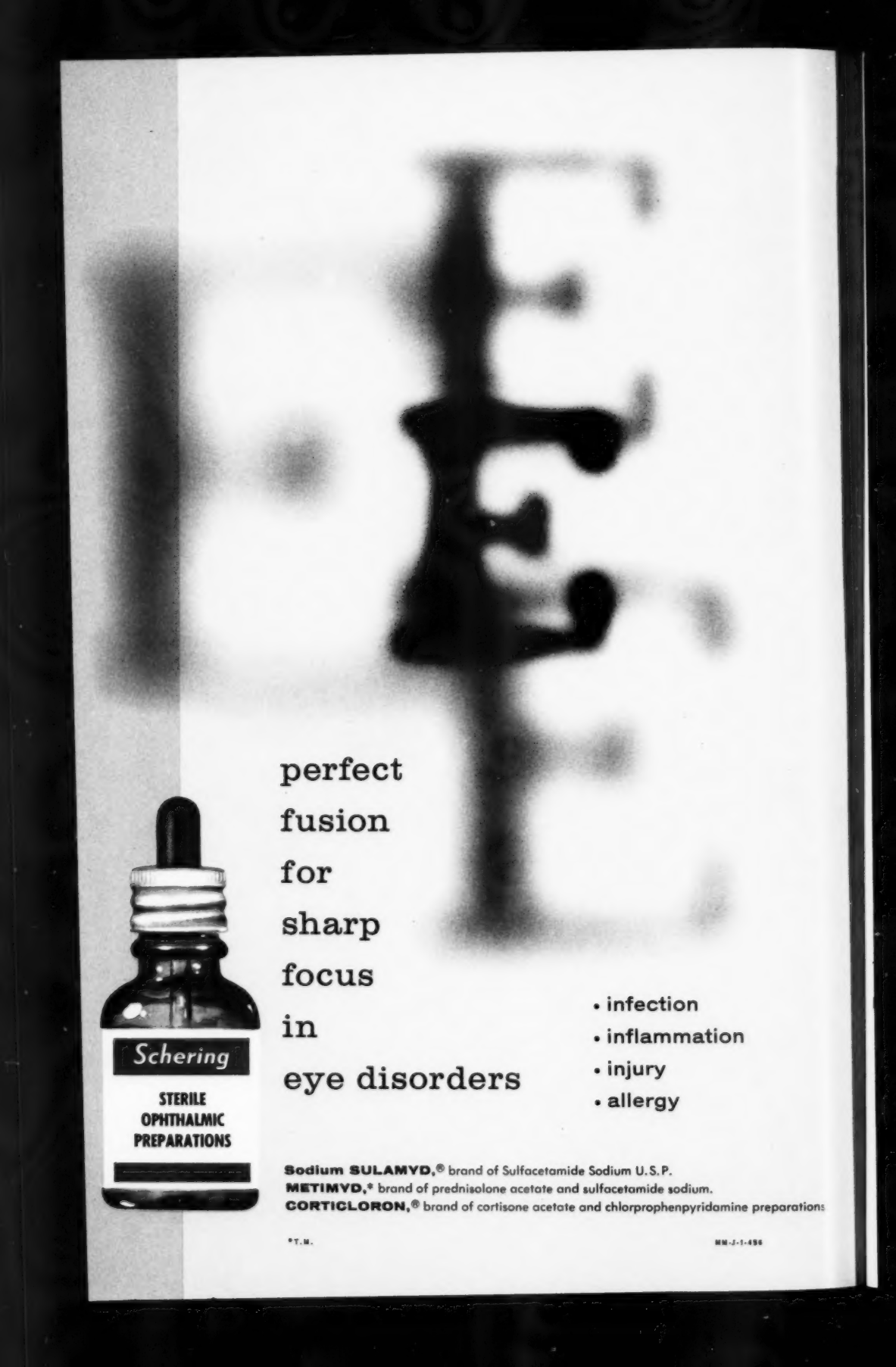
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